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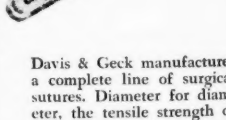
references:

1. A. W. Spittler, Col., (M.C.), U.S.A., J. J. Brennan, Lt. Col., (M.C.), U.S.A., J. W. Payne, Capt., U.S.A.F. (M.C.), American Academy of Orthopedic Surgeons, Jan. 26-31, 1952, Chicago, Illinois.
2. M. C. Cobey, M.D., F.A.C.S., Professor of Orthopedic Surgery, Georgetown University and Senior Attending Orthopedic Surgeon, Children's Hospital, Washington, D.C., The American Surgeon, Vol. XVIII, No. 4, April, 1952, pp. 413, 415.
3. M. C. Cobey, M.D., F.A.C.S., Washington, D.C., private communication.



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SURGERY
GYNECOLOGY AND OBSTETRICS

VOLUME 95 NOVEMBER, 1952 NUMBER 5

EFFECTS OF VAGOTOMY ON PANCREATIC SECRETION IN DOGS WITH CHRONIC PANCREATIC FISTULA

ERIC F. ROUTLEY, M.D., FRANK C. MANN, M.D., JESSE L. BOLLMAN, M.D., and JOHN H. GRINDLAY, M.D., Rochester, Minnesota

EXTERNAL pancreatic secretion was studied in dogs with chronic total pancreatic fistulas, particular attention being given to the effects of vagotomy on external pancreatic function. The investigation was undertaken with two main purposes in mind: (1) to study numerous experimental conditions or factors which may influence external pancreatic secretion and (2) to determine the effects of vagotomy, if any, on external pancreatic function in the dog.

The scope of the investigation was limited to studies on external pancreatic function in healthy, trained dogs, weighing 12 to 20 kilograms, all of which had chronic total pancreatic fistulas, most of which also had gastric fistulas and some of which were also vagotomized.

The pancreatic secretion in response to sixteen experimental conditions (or stimuli), before and after vagotomy, was evaluated by the following determinations: the rate of flow (volume in milliliters per hour), concentration of amylase, lipase and trypsin, and specific gravity. Studies of protein, chloride, and bicarbonate contents were omitted. Gastric secretion was not excluded from the duodenum, in order to simulate as closely as possible the usual anatomic and physiologic conditions pertaining to pancreatic secretion in normal and vagotomized human subjects. Gross and microscopic studies were made on necropsy material with special reference to the completeness of vagotomy and the possible effects of vagotomy on the pancreatic islet cell tissue.

In the voluminous literature on vagotomy, pancreatic physiology, enzymes, and related subjects, there is very little specific reference to any effects of vagotomy on pancreatic secretion. It had been suggested by one group of investigators (6) that the persistent diarrhea commonly noted in vagotomized patients might be due to some disturbance of external pancreatic function as a result of the vagotomy. In general, however, the impression gained from a review of some 300 articles is that vagotomy has no significant side effects on the liver, gallbladder, spleen, or pancreas, and that herein lie no contraindications to therapeutic vagotomy.

The control of external pancreatic secretion is based, in essence, on three mechanisms: (1) the secretin mechanism, which provokes secretion of watery pancreatic juice of great volume, rich in bicarbonate and low in enzymes, (2) the pancreozymin mechanism, which causes outpouring of the pancreatic enzymes, and (3) the nervous mechanism (mediated through the vagus nerves and probably

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Abridgment of thesis submitted by Dr. Routley to the Faculty of the Graduate School of the University of Minnesota in partial fulfillment of the requirements for the degree of Master of Science in Surgery.

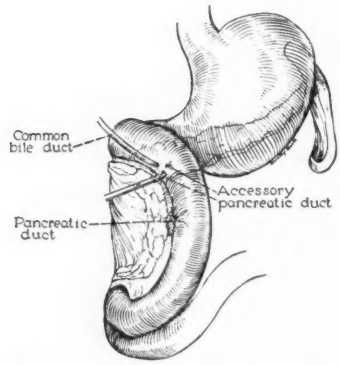

Fig. 1. The accessory pancreatic duct, exposed by reflecting the duodenum anteromedially, enters the duodenum in the dog in very close association with the common bile duct. It is avulsed as described in text.

some cholinergic sympathetic fibers); the role of the vagal mechanism, in the functional innervation of the pancreas, has been suggested by Thomas and associates (2, 8) to be that of a "tonus" mechanism which may augment or inhibit local reflexes.

METHODS

Chronic total pancreatic fistula. This was prepared in 30 dogs, employing a modification of pancreatic duct cannulation described by Elman and McCaughan and more recently by Baggenstoss, Power, and Grindlay. After avulsion of the accessory pancreatic duct, which in the dog lies orad in association with the common bile duct (Fig. 1), the main pancreatic duct is cannulated with polyvinyl resin plastic tubing (Figs. 2 and 3). Our modification of the previously described technique consists of placing two small collars, made of the same plastic tubing, around the pancreatic cannula to aid in fixation. One of these collars is about 5 millimeters from the beveled tip of the cannula where it enters the slit in the main pancreatic duct; by means of one or two black silk sutures threaded under this collar and through the anterior wall of the duct the cannula can be tied snugly into the duct. The other plastic collar is placed about 15 centimeters from the tip of the cannula, at the point where it leaves the peritoneal cavity through a small stab wound in the upper right portion of the abdomen, and is utilized in similar fashion for fixation by one or two black silk sutures tied to the adjacent parietal peritoneum. These collars are only 2 to 3 millimeters in length and are the size of tubing which will just fit snugly over the cannula (example: cannula size 20, collar size 18). Care is taken not to split the collar or perforate the cannula while passing the silk sutures beneath the collar. The exteriorized portion of the pancreatic cannula is cut obliquely about 10 centimeters beyond the exit through the skin.

Gastric fistula. A fistula of a modified Witzel gastrostomy type was prepared in 22 of the 30 dogs. The fistula is tunneled through the musculature of the anterior wall of the antrum and the cannula is directed toward the pyloric sphincter (Fig. 4). The polyvinyl resin cannula is of the (next larger) size into which the pancreatic cannula fits snugly. This cannula also has two plastic collars placed at fixation points (1) where it leaves the serosal end of the wound in the stomach and (2) where it leaves the parietal peritoneum through a stab wound in the left upper portion of the abdomen. The cannula has an intra-abdominal loop of about 15 centimeters and an exteriorized segment (cut transversely) about 10 centimeters beyond the skin.

At the conclusion of the operation, a firm collar the length of the dog's neck is buckled in place to prevent him from chewing on the tubes.

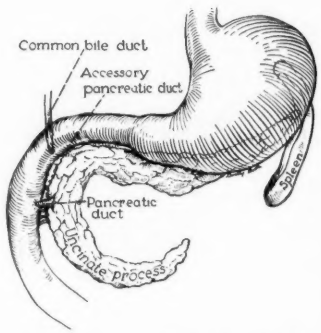

Fig. 2. The main pancreatic duct enters the duodenum anteromedially about 2.5 centimeters distal to the accessory duct, in the leash of vessels forming the most distal point of intimate attachment of the head of the pancreas to the duodenum.

The exteriorized segments of the two cannulas are conveniently formed into a shunt by fitting the slightly smaller (and beveled) end of the pancreatic tube into the terminal 1 to 2 centimeters of the larger gastric tube (which may be slightly dilated with a small hemostat to facilitate the connection). The loop thus formed is protected by some gauze and a muslin coat made to fit each dog. Whenever it is desired to collect pancreatic juice the loop is disconnected and the gastric cannula is plugged (with a golf tee or wooden match stick), while secretion flows freely from the pancreatic cannula. By means of the shunt, between collections, pancreatic juice is constantly returned to the gastrointestinal tract (through the stomach), which is of utmost importance in the maintenance of dogs with chronic pancreatic fistula. Total loss of external pancreatic secretion for more than 7 to 10 days results in marked fluid and electrolyte imbalance and a downhill course with fatal termination, unless most of the juice is returned to the dog, formerly by stomach tube or with a meal. None of our dogs receiving most of their pancreatic juice through the shunt required any other specific measures for maintenance in this respect.

The gastric fistula also provides a channel for the introduction of various foods and stimuli such as alcohol, bile, olive oil, hydrochloric acid, and so forth (see experimental conditions). Rarely, after a big meal, the pancreatic juice did not flow well into the gastric limb of the shunt, presumably owing to increased pressure in the stomach, but at all other times the pressure of pancreatic secretion carried the juice in the desired direction (toward the stomach).

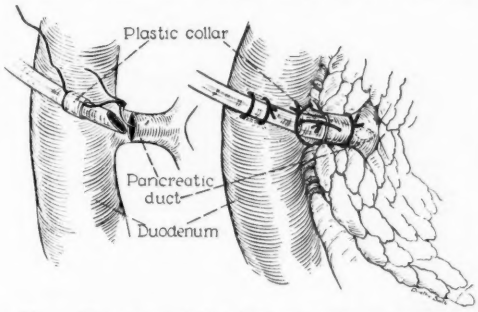

Fig. 3. The pancreatic fistula is prepared by cannulating the main pancreatic duct with polyvinyl resin (transflex) plastic tubing in the detailed manner described in the text.

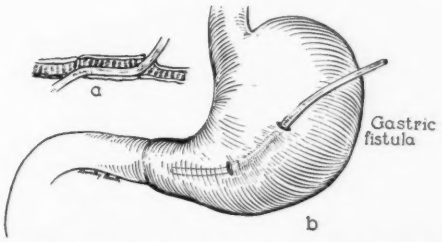

Fig. 4. A gastric fistula of modified Witzel gastrostomy type is prepared with polyvinyl resin (transflex) plastic tubing of a size large enough to permit snug entrance of the end of the pancreatic cannula to form an external shunt (see text).

These preparations of pancreatic and gastric fistula functioned well for several weeks, and in some cases for 2 to 3 months.

Vagotomy. This was performed on 9 of the dogs. Complete supradiaphragmatic vagotomy, through the left side of the thorax, consisted of removal of both vagus nerves and their ramifications between the hilus of the lungs and the diaphragm, including any palpable or visible intramural esophageal branches or trunks.

Determinations on pancreatic juice. 1. Volume.—The rate of flow in milliliters per hour was measured.

2. Amylase activity (concentration).—This was determined by Lagerlöf's starch hydrolysis and expressed as grams of maltose per milliliter of pancreatic juice.

3. Lipase activity (concentration).—This was determined by the hydrolysis of an olive oil emulsion and titration of the fatty acids liberated with tenth-normal alcoholic potassium hydroxide, by which value it was expressed.

4. Trypsin activity (concentration).—This was determined, after activation of the trypsinogen with enterokinase, by the hydrolysis of denatured bovine hemoglobin; the tyrosine liberated was determined colorimetrically and the trypsin activity was expressed as milligrams of tyrosine per milliliter of pancreatic juice.

5. Specific gravity.—(This may be used as an indication of protein content.) It was de-

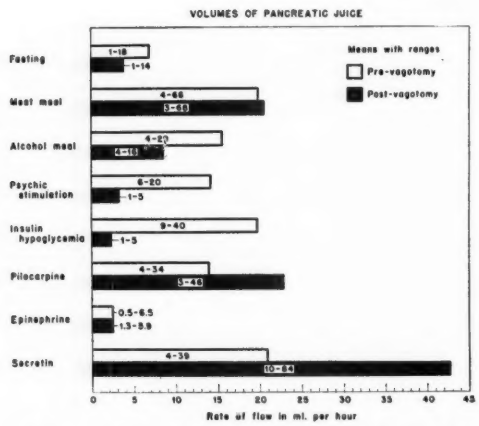

Fig. 5. Volumes of pancreatic secretion in some of the experimental conditions used in the study, before and after vagotomy, with mean values represented by the bar diagram and ranges indicated within each bar.

termined by means of a standard hydrometer on specimens of pancreatic juice which were of adequate volume (15 ml. and more).

Pancreatic juice was collected on ice and preserved by refrigeration and the addition of an equal volume of glycerin.

The sixteen experimental conditions or stimuli under which pancreatic secretion was studied, before and after vagotomy, were as follows: (1) fasting state, (2) meat meal, (3) liquid diet, (4) standard diet, (5) olive oil, (6) bile, (7) hydrochloric acid, (8) alcohol, (9) psychic stimulation (a type of "sham feeding"), (10) insulin hypoglycemia, (11) methacholine (mecholyl) subcutaneously, (12) pilocarpine subcutaneously, (13) epinephrine intravenously, (14) histamine subcutaneously, (15) secretin intravenously, and (16) pancreozymin (plus secretin) intravenously. Stimuli 5, 6, 7, and 8 were put into the stomach in aqueous solution through the gastric fistula. The details of these methods are discussed in the thesis (7).

Necropsy studies included search for anatomic evidence of completeness of the vagotomy and for duodenal ulcers; the pancreas was studied and special stains (Gömöri) were used in order to study possible changes present in the islet cells of the pancreas in vagotomized dogs.

RESULTS

Satisfactory pancreatic fistulas were established in 30 dogs, 22 of which also had gastric fistulas, and 9 of which were also vagotomized. The majority of the pancreatic fistulas functioned 3 to 4 weeks, and a few flowed for 8 to 10 weeks. The usual reason for cessation of function was dislodgement of the cannula from the pancreatic duct, in spite of most painstaking efforts to establish good fixation during the operation. However, exploration or necropsy of such animals generally revealed that the opening in the duct at the site of cannulation had closed, thus permitting juice to enter the duodenum normally, or new channels had formed by which pancreatic juice was draining into the adjacent duodenum. In most dogs the pancreas appeared normal, although atrophy was noted in a few cases.

About 450 experiments before vagotomy and 315 experiments after vagotomy provided some 1,100 collections of pancreatic juice in all of which rate of flow was noted, and on which duplicate or triplicate determinations of amylase, lipase, and trypsin were made; about one third of the samples were of sufficient volume to permit determination of specific gravity.

The abundant data on volume, enzymes, and specific gravity were studied statistically.

Some typical experimental results are indicated in bar diagrams in Figures 5, 6, and 7.

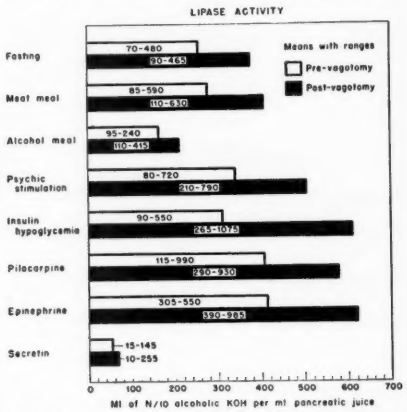

Fig. 6. Lipase activity represented in similar manner for the same group of experiments as indicated in Figure 9. Values for amylase and trypsin are omitted here.

In these bar diagrams the wide ranges of values for volume and enzyme (trypsin) are noted (inserted within each bar), in order to illustrate the marked variability in pancreatic secretion from one dog to another and in the same dog from day to day, under experimental conditions which were controlled as carefully as possible. Because of such variations many experiments were necessary to collect sufficient data for reliable statistical analysis. The mean values, indicated by the length of the bars, show the relative responses of pancreatic secretion to various stimuli in a representative group of the sixteen experimental conditions, and provide an estimate of the effects of vagotomy by a comparison of light and dark bars.

The data in more complete form are represented in bar diagrams of Figures 8, 9, and 10. The pancreatic secretion of fifteen of the experimental conditions are compared with the fasting values (the fasting state being the sixteenth experimental condition) in terms of mean per cent increase or decrease, before and after vagotomy (light and dark bars).

The results of the statistical analysis of the effects of vagotomy on pancreatic secretion are presented in Table I.

From the data the following generalizations appear warranted:

1. Volumes (rate of flow) of pancreatic secretion before vagotomy were greatest, in order of decreasing magnitude, in response to secretin, histamine, hydrochloric acid and meals (through the secretin mechanism of external pancreatic secretion). Only epinephrine caused diminished volumes. Postvagotomy volumes were particularly high after the use of methacholine, pilocarpine, secretin, and pancreozymin.

2. The concentrations of enzymes before vagotomy were greatest in response to pilocarpine, methacholine, olive oil, psychic stimulation, and epinephrine (through the nervous and pancreozymin mechanisms of external pancreatic secretion). There was marked parallelism in the activity of the three enzymes—amylase, lipase, and trypsin—regardless of the stimulus. Postvagotomy enzyme concentrations were relatively low in response to methacholine, pilocarpine, pancreozymin and secretin.

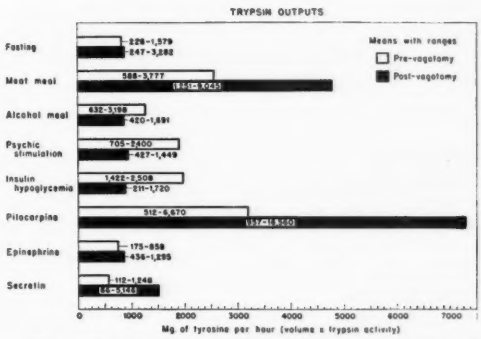

Fig. 7. Trypsin output (volume × activity) represented in similar manner for the same experiments as in Figures 9 and 10. Values for amylase and lipase are omitted in this diagram.

3. Enzyme output (calculated from enzyme activity multiplied by hourly volume), which represents the best criterion for evaluation of external pancreatic function, was again noted in marked parallelism for the three enzymes. Following the use of secretin and epinephrine enzyme output was essentially that of the fasting state. Thus the effect of secretin was to provoke a very voluminous but watery secretion poor in enzymes; thus secretin does not stimulate enzyme production but merely "washes out" enzymes being formed at the same rate as in the fasting state. Epinephrine caused a scanty flow rich in enzymes, the enzymes apparently again being formed at the same rate as in the fasting state. Enzyme outputs before vagotomy were greatest in response to pilocarpine, methacholine, meat and other meals, psychic stimulation, insulin hypoglycemia, and pancreozymin. The only instances in which vagotomy caused diminished output of enzymes (Table I) were in experiments using insulin hypoglycemia and psychic stimulation. The slightly diminished response to bile was not statistically significant. Vagotomy produced increased enzyme outputs in response to meat (and other) meals, pilocarpine, epinephrine, secretin, and pancreozymin.

Alcohol provoked only moderate increases in volume and enzyme activity of pancreatic secretion (see comment).

4. Only statistically significant effects of vagotomy are shown in Table I. None of the

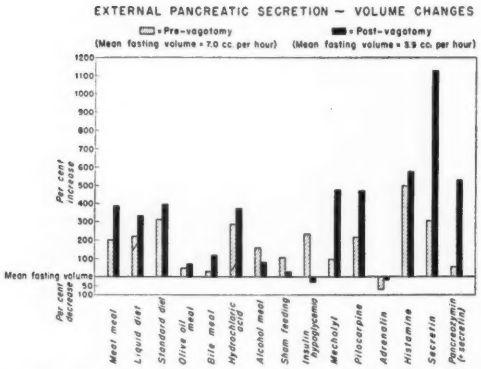

Fig. 8. Rate of flow (volume) of pancreatic secretion is represented by bar diagrams. Prevagotomy and post-vagotomy values after each stimulus are compared with the fasting volumes, in terms of per cent increase or decrease.

TABLE I.— EFFECTS OF VAGOTOMY ON EXTERNAL PANCREATIC FUNCTION*

Pancreatic function	Response after vagotomy	
	Increased	Decreased
Volume (rate of flow)	Methacholine Secretin Pancreozymin (+ secretin)	Psychic stimulation Insulin hypoglycemia Epinephrine Fasting state
Enzyme activity (concentration)	Fasting state	Methacholine Secretin Pancreozymin (+ secretin)
Enzyme output (volume × activity)	Meat meal Secretin Pancreozymin (+ secretin) (Liquid diet†)	Psychic stimulation Insulin hypoglycemia

*Statistical analysis of all data revealed that vagotomy produced significant increase or decrease in pancreatic secretion under only the few experimental conditions noted.
†Vagotomy resulted in increased output of amylase in response to a liquid diet, but no significant increase in output of lipase or trypsin.

other previously stated, apparent effects of vagotomy were statistically significant. Enzyme outputs following the ingestion of meat and administration of secretin and pancreozymin were increased by vagotomy (see comment). The increased volumes in response to methacholine, secretin, and pancreozymin, due to vagotomy, were accompanied by reciprocal decreases in enzyme activity. The reverse held true for these values in the fasting state—that is, vagotomy produced a decrease in volume but an increase in enzyme activity of pancreatic juice, with a resultant insignificant effect on enzyme output (see comment).

Specific gravity studies were not contributory; values were poorly correlated and specimens were frequently of insufficient volume to get readings.

Studies at necropsy revealed no peptic ulcers, good gross and microscopic evidence of completeness of the vagotomy, and no changes in the pancreatic islet or acinar cells following vagotomy.

COMMENT

It is believed that cannulation of the main pancreatic duct with polyvinyl resin plastic tubing for the establishment of a chronic total pancreatic fistula, and the return of noncollected pancreatic secretion through a gastric fistula (through a simple external shunt), provides a very satisfactory method for studies of external pancreatic secretion in trained dogs, under a wide variety of experimental conditions, over periods of weeks or months.

Our results conformed well to the concept of the three basic mechanisms controlling external pancreatic secretion: secretin, pancreozymin, and nervous mechanisms. The finding that vagotomy had essentially no significant effect on pancreatic function fits in with the hypothesis that the role of the vagus nerves in the control of external pancreatic secretion is

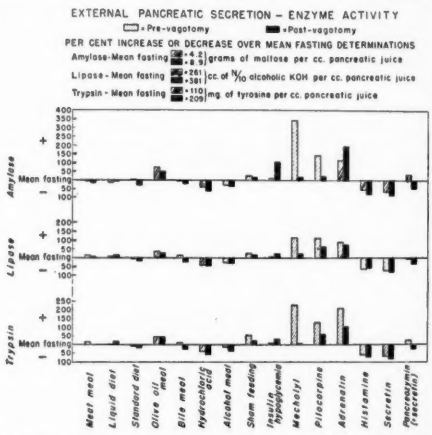

Fig. 9. Enzyme activity (concentration) is represented by bar diagrams and compared with fasting values in the same manner as comparison of volumes. The marked parallelism in the values for the three enzymes is noted; hence, the study of any one of the three would provide satisfactory data on enzymes.

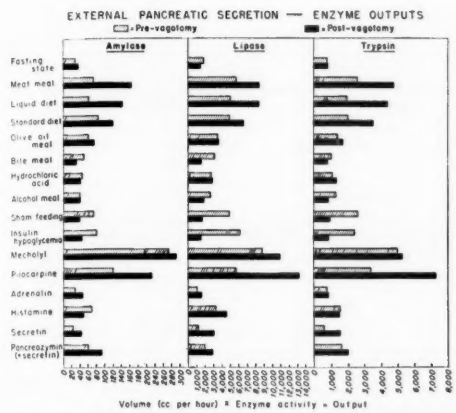

Fig. 10. Enzyme output (volume × activity), compiled from the data represented in Figures 8 and 9, is similarly represented and compared. Parallelism is again noted. The dark bars, representing the postvagotomy values, provide a rapid visual appraisal of the effects of vagotomy on pancreatic secretion in each of the experimental conditions, by comparison with the light bars (the prevagotomy values of enzyme output).

that of a "tonus mechanism which may augment or inhibit local reflexes."

The findings confirmed the impression gained from the literature that vagotomy has no significant side effects on the pancreas. Hence, it is very unlikely that the diarrhea commonly encountered in vagotomized human beings is on a basis of disturbed pancreatic function.

The marked parallelism in the activity of the three pancreatic enzymes, regardless of the stimulus, denies the ancient concept of enzyme adaptivity according to the stimulus employed (for example, the lipase activity being relatively increased after fatty meals). This observation provides evidence in favor of limiting a study of pancreatic enzymes to any one of the three (for example, only trypsin determinations).

The minimal pancreatic secretion provoked by alcohol in the dog is in contrast to the notoriously marked effects of alcohol in precipitating attacks of chronic relapsing pancreatitis in man.

After vagotomy, the increased enzyme outputs following the use of a meat meal, secretin and pancreozymin may well be on a basis of released vagal tonus mechanism permitting hyperactivity of local reflexes. Vagotomy produced no effects on enzyme output in the fasting dog, which probably represents the most significant experimental condition under which to study effects of a nerve-cutting procedure on external pancreatic secretion. The diminished enzyme outputs, after vagotomy, in response to insulin hypoglycemia and psychic stimulation, are explained on the basis of the diminished gastric secretion known to follow vagotomy. The inhibitory effects of epinephrine on pancreatic secretion are thought to be on a basis of vasoconstriction.

SUMMARY AND CONCLUSIONS

External pancreatic secretion was studied in 30 dogs with chronic total pancreatic fistulas, 22 of which had gastric fistulas and 9 of which were vagotomized. We were particularly interested in the effects of vagotomy on pancreatic function. The data obtained from about 450 experiments before vagotomy and 315 experiments after vagotomy, measuring volume, enzymes, and specific gravity of about 1,100 samples of pancreatic juice, collected under a variety of stimuli, were studied statistically and are presented in very brief form by bar diagrams. The results are discussed in some detail. Factors which enhance and diminish external pancreatic secretion are considered.

1. Stimuli which provoke the production of copious volumes of pancreatic secretion (through the secretin mechanism) include secretin, histamine, hydrochloric acid, and meals. Epinephrine was the only stimulus which diminished the rate of flow of pancreatic juice in this study.

2. Stimuli which increase enzyme activity (through the nervous and pancreozymin mechanisms) include pilocarpine, methacholine, olive oil, and psychic stimulation.

3. The three enzymes—amylase, lipase, and trypsin—are secreted in markedly parallel concentrations, regardless of the nature of the stimulus.

4. Alcohol is not a powerful stimulant of canine pancreatic secretion, as opposed to its notorious effects in the human subject.

5. We are inclined to favor the hypothesis that the vagus control of pancreatic secretion

is that of a tonus mechanism which may augment or inhibit local reflexes.

6. Under the experimental conditions employed in this investigation, in trained dogs, vagotomy produced no significant effects on external pancreatic secretion.

REFERENCES

1. Baggenstoss, A. H., Power, M. H., and Grindlay, J. H. The extraction of secretin from the intestine of man; absence of secretin in a case of fibrocystic disease of the pancreas. Gastroenterology, 1948, 11: 208–220.
2. Crider, J. O., and Thomas, J. E. Secretion of pancreatic juice after cutting extrinsic nerves. Am. J. Physiol., 1944, 141: 730–737.
3. Elman, R., and McCaughan, J. M. Collection of entire external secretion of pancreas under sterile conditions and fatal effect of total loss of pancreatic juice. J. Exp. M., 1927, 45: 561–570.
4. Gömöri, G. Observations with differential stains on human islets of Langerhans. Am. J. Path., 1941, 17: 395–406.
5. Lagerlöf, H. O. Pancreatic Function and Pancreatic Disease, Studied by Means of Secretin. New York: The Macmillan Co., 1942.
6. Pincus, I. J., Thomas, J. E., and Lachman, P. O. The effect of vagotomy on the secretion of pancreatic juice after the ingestion of various foodstuffs (preliminary report). Fed. Proc., Balt., 1948, 7: 94.
7. Routley, E. F. Effects of vagotomy on pancreatic secretion and a method for chronic pancreatic fistula. Thesis, Univ. of Minnesota Grad. Sch., 1952.
8. Thomas, J. E., and Komarov, S. A. Physiological aspects of vagotomy. Gastroenterology, 1948, 11: 413–418.

THE DISTRIBUTION OF VALVES IN THE FEMORAL, EXTERNAL ILIAC, AND COMMON ILIAC VEINS AND THEIR RELATIONSHIP TO VARICOSE VEINS

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FOR many years the absence of valves in the main veins of the lower extremities (femoral and iliac) has been regarded as important in the etiology of varicose veins. The accepted theory states that if there are no valves above the mouth of the long saphenous vein the hydrostatic pressure will be greater in this vein and so cause or accelerate the production of varicosities. It is a common observation that valves are usually found in the region of the inguinal ligament, but the standard textbooks disagree on the disposition of these and other valves. Indeed, several statements are found which are misleading. The original but brief report on these valves was by Friedreich in 1882, and it appears that many textbooks either quote or paraphrase his results.

In the past 30 years a number of excellent papers have appeared from various centers regarding the gross arrangement of the veins of the lower limb and their anastomoses. The many valves in the long saphenous vein and their development also have been thoroughly investigated and reported. Yet, only brief reports by Eger and Caspar in 1943 (3) and by Eger and Wagner in 1949 (4) have dealt specifically with all the valves above the saphenofemoral junction. These investigators had a definite problem in mind—the cause of saphenous varices—so they did not deal with the distal parts of the femoral vein. In 1911, Hesse and Schaak (7) investigated the saphenous and the femoral veins but not the external iliac.

It has been accepted generally that there are no valves above or proximal to the external iliac veins (i.e., in the common iliac and inferior vena cava). Friedreich and later McMurrich (11) and Di Dio (2) have each reported the occurrence of valves in the common iliac vein.

Anatomy textbooks state that there are 1 or 2 valves in the external iliac vein. These statements are presumably based on the work of Friedreich who found 35 per cent of external iliac veins contained a valve. He considered that about ⅓ of these valves were incompetent. His work is generally quoted by the German, French, British, and American authors, apparently in that chronological order. Friedreich reported that 80 per cent of femoral veins had valves in the upper 5 centimeters. He also stated that constantly there was a good valve just above the profunda tributary. It will be shown that this last statement was erroneous.

MATERIAL AND METHOD

A series of 38 dissecting room subjects (76 paired limbs) was investigated at the University of Toronto. In 2 subjects the iliac vessels had been destroyed leaving only the femoral veins suitable for study. All of the subjects were males and their ages ranged from 31 to 94 years, most of them being over 50 years of age.

The common and external iliac veins and the femoral vein (to where it passes through the hiatus in the adductor magnus) were split open in situ. The level and characteristics of each valve were recorded on a special blank form. In an external iliac vein the distance of each valve was measured in centimeters from either the mouth of the internal iliac (hypogastric) vein or the inguinal ligament of Poupart, whichever was closer. In the case of the femoral valves, measurement in centimeters proceeded from the inguinal ligament

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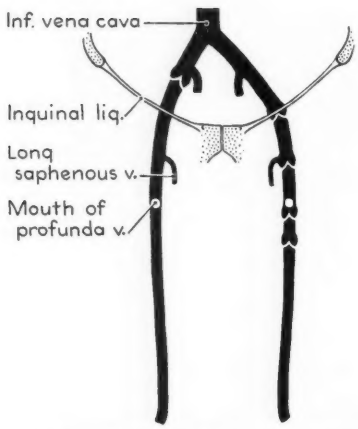

Fig. 1. An unusual pattern of distribution of valves in the femoral, external iliac and common iliac veins (male subject, aged 63 years).

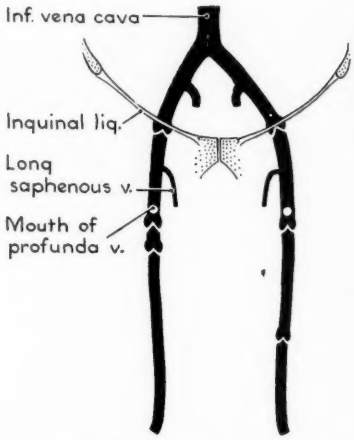

Fig. 2. A common pattern of distribution of valves in the femoral, external iliac and common iliac veins (male subject, aged 94 years).

where it is crossed by the main venous trunk. Since neither the inguinal ligament nor the main venous trunk can be identified accurately from the skin surface, equivalent figures would be obtained in living subjects by measuring vertically downward from the pubic tubercle (spine) and subtracting about 2 centimeters.

Special attention was paid to the valves in the main femoral vein near the mouth of its profunda tributary. The level of the mouth of the profunda tributary was also noted.

The superficial and deep veins of the limbs were examined for gross evidence of varicosities.

RESULTS

Valves above the mouth of the long saphenous vein. In 72 venous trunks, where both iliac and femoral veins were examined, 15 (20.8 per cent) had no valves above the level of the long saphenous, 51 (70.8 per cent) had 1 valve, 5 (7 per cent) had 2 valves, and 1 (1.4 per cent) had 3 valves. Most of these valves were in the femoral vein, although in 11 limbs (12.5 per cent) there was a valve in the external iliac vein but none in the femoral above the entrance of the saphenous tributary.

Valves in the common iliac vein. None of the 72 common iliac veins in this series contained a valve.

Valves in the external iliac vein. Sixteen of the 72 external iliac veins (22.2 per cent) contained a single valve (not including valves at or just below the inguinal ligament). Twelve of these valves were within 3 centimeters of the mouth of the internal iliac vein, and the remaining 4 were within 3 centimeters of the inguinal ligament. Thirteen were on the right side and 3 on the left. All but 4 (i.e., 3/4) of the valves in this series appeared to be competent on macroscopic examination. Admittedly, the estimation of the competence of valves in a dissected vein may be fallacious. Criteria used required large well formed cusps which could meet and prevent retrograde flow.

Valves in the femoral vein. (a) At or just below the inguinal ligament. Twenty-three right and 28 left femoral veins, i.e., 51 of a total of 76 (67.1 per cent or about 2/3), had a valve at or within 5 centimeters of the inguinal ligament. Such a valve was found bilaterally in about half of the cadavers (18 of 38). Most of these valves (42 of the 51) were within 1 centimeter of the inguinal ligament, 5 were within 3 centimeters of the ligament, and 4 were within 5 centimeters of the ligament and just above the mouth of the long saphenous tributary.

(b) Below the mouth of the long saphenous vein. It is in this segment of the main venous

trunk that the distribution of valves has been described incorrectly by many authors.

In the 38 subjects (76 paired limbs) of this series there was one right limb with no valves in the femoral vein throughout, although there was a good valve in the external iliac 1 centimeter below the mouth of the internal iliac vein. In the opposite femoral vein there were 4 good valves (Fig. 1). None of the veins of either limb had varicosities.

Contrary to the textbook descriptions based on Friedreich's early paper, a valve immediately above the mouth of the profunda femoris was rare. In this investigation, only one vein (1.3 per cent) possessed a valve in this location. In one other vein there was a valve 4 centimeters above the mouth of the profunda tributary and just below the saphenofemoral junction (Fig. 1).

The most constant site for a valve in the femoral vein was just below or distal to the mouth of its profunda tributary. This occurred in 68 of the 76 femoral veins, an incidence of 89.5 per cent, and was usually bilateral (in 29 of 36 subjects). Most of the valves (59 of the 68) were less than 1 centimeter distal to the opening of the profunda tributary into the femoral vein. The remaining 9 valves were not more than 3 centimeters distal to the mouth of this tributary.

The average distance of the mouth of the profunda femoris vein from the inguinal ligament was 9 centimeters. Almost all were between 8 and 11 centimeters from the ligament.

(c) Total number of valves in the femoral vein between the mouth of the profunda tributary and the hiatus in the adductor magnus. In this segment, 5 veins (6.6 per cent) had 5 valves, 9 veins (11.9 per cent) had 4 valves, 24 veins (31.7 per cent) had 3 valves, 23 veins (30.4 per cent) had 2 valves, 13 veins (17.2 per cent) had 1 valve, and 2 veins (2.6 per cent) had no valves. There was no definite pattern of bilateral symmetry of position or of number.

(d) Total number of valves in the femoral vein. The number of valves in the main trunk from the inguinal ligament to the hiatus in adductor magnus varied from none (in 1 case or 1.3 per cent) to 6 (in 5 cases or 6.6 per cent). Six femoral veins (7.9 per cent) had 1 valve; 18 (23.8 per cent) had 2 valves; 25 (33 per cent) had 3 valves; and 3 veins (3.9 per cent) had 5 valves.

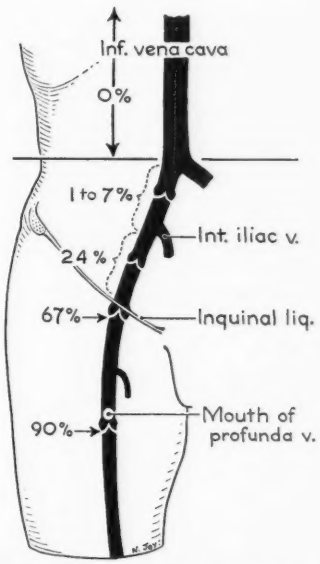

Fig. 3. Incidence of valves in the inferior vena cava, common iliac and external iliac veins, and at two special sites in the femoral vein.

Character of the valves. Almost all of the valves were bicuspid with one cusp anterior and the other posterior. The great majority were large and on macroscopic examination appeared to be competent. One external iliac vein contained a single, very large posterior cusp which appeared to be quite sufficient. Another contained an excellent tricuspid valve. A small, incompetent unicuspid valve was seen only twice in the femoral vein.

Presence of varicose veins. There were two limbs from separate subjects in which varicose veins were found. The first had a grossly varicose long saphenous vein below the level of the knee. The main venous trunk of this right lower limb had a good valve 3 centimeters above the inguinal ligament and 2 valves in the femoral vein 1 and 3 centimeters below the mouth of the profunda tributary. The long saphenous vein was opened and 5 valves were found along its length. The upper 3 were large and apparently competent; the

lower 2 were incompetent and involved in the varicose portion of the vein. The second limb —a left sided one—had a short saphenous vein that was grossly dilated and tortuous for about 8 centimeters of its upper end. The main venous trunk of this limb had 2 valves, which appeared competent. The upper valve was 1 centimeter below the mouth of the profunda tributary and the other was in the popliteal vein about 7 centimeters above the mouth of the varicose short saphenous vein.

DISCUSSION

Relationship of the absence of valves in the main venous trunk to the cause of varicose veins. The present group of cases was studied with the problem of the cause of varicose veins in mind. The contention has been that the absence of valves in the main trunk veins above the mouth of the long saphenous vein is an important factor in the etiology of saphenous varices. Eger and Wagner (4) studied the valvular distribution above the saphenofemoral junction in specimens removed from 100 cadavers. They reported the total absence of valves on one or both sides in 42 subjects and concluded that, "there is a 42 per cent minimal incidence of increased stress at the saphenofemoral junction" and that, ". . . this is a potential etiologic factor in the development of varicose veins." No note, however, was made as to the presence or absence of varicose veins in these subjects.

In our present series of 72 limbs in which the veins were intact above the saphenofemoral junction, only 15 (20.8 per cent) had no valves in this segment. Powell and Lynn who studied the main venous trunk and its valves found that in 25 per cent of 54 limbs there were "no valves whatsoever . . . between the heart and the mouth of the long saphenous vein." Lynn states that in the remaining 75 per cent of cases 4/5 appeared to be incompetent (admitting the difficulty in the assessment of competence after dissection). In general terms, then, about every second person should be a potential sufferer from varicose veins, if the theory of absence of valves above the saphenofemoral junction is valid.

Only one previous report has dealt with both the occurrence of valves and of varicosities. Hesse and Schaak (7) examined the femoral and saphenous veins of 100 random adult limbs. Four of the cases had varicose veins. Of these cases 1 had a good valve, 2 had a poor valve, and the fourth had no valve in the femoral vein above the saphenofemoral junction. The failure to examine the external iliac veins partially invalidates these results. On the other hand, the results themselves support our own.

A very pertinent finding in our series, of course, is that serious varicosities were present in one long saphenous vein in a limb with an excellent large valve in the external iliac vein. Another important finding was the presence of 2 apparently competent valves above the mouth of the varicose short saphenous vein in another limb. Furthermore, among the 20 per cent of limbs without valves above the saphenofemoral junction, no varicose veins were found. These occurrences are embarrassing to the theory already stated. They would appear to cast considerable doubt on its validity.

It is noteworthy that the occurrence of 2 varicose veins in 36 adult males is not unusual and is in general agreement with the statistical findings in the population. Ochsner and Mahorner reported that 3 per cent of 9,000 patients admitted to the Hutchison Memorial Clinic had varicose veins. Much higher and lower percentages have been quoted by other authors. Hesse and Schaak (7) found 4 per cent of 100 random adult lower limbs had saphenous varices on anatomical examination.

The frequency of valves in the iliac and femoral veins. The common iliac vein.—Judging from the detailed work of Di Dio (2), the common iliac vein not rarely contains a valve (7 per cent), but almost all the valves in this vein are quite small and incompetent. Friedreich and McMurrich have also reported the occasional occurrence of valves in the common iliac vein. The former reported that 5 veins in 370 had valves. The latter found that 2 common iliac veins in the 60 that he examined were valved.

Ehrich and Krumbhaar, after examining a long series of autopsy cases of all ages, reported the presence of a small cusp-like structure (which they called a "valve") at the

upper end of many of the common iliac veins. It was "found to be normally present in the newborn . . . but it appeared to be worn off in an ever greater percentage as age progressed."

Worthy of mention here is the work done by Ehrich and Krumbhaar and more recently by Di Dio (1, 2) in studying the interior of the common iliac veins. These investigators have examined hundreds of cases to confirm J. P. McMurrich's original observation in 1906 (11, 12) of intimal adhesions in these veins. The commonest site for such adhesions is the retroarterial part of the left common iliac vein. The suggestion is made that the greater frequency of venous thromboses in the left lower limb may be due to the presence of these adhesions.

The external iliac vein.—Friedreich found valves in 29.5 per cent of 370 veins; Eger and Wagner found a 22 per cent incidence in 200 veins; Powell and Lynn found a 33 per cent incidence in 54 limbs. The incidence in the present series of 72 limbs is 22 per cent. When the totals of the four series are combined there is a valve in 24 per cent of external iliac veins. That is, about 1 in 4 external iliac veins contains a valve. More than ⅔ of these are competent.

The femoral vein.—The present series shows that rarely (1.3 per cent) is there no valve in the whole length of the femoral vein. Uncommonly there are as many as 6 valves (in 6.6 per cent) or as few as 1 (in 7.9 per cent). Most of the veins contain 2 valves (23.8 per cent), 3 valves (33 per cent), or 4 valves (23.8 per cent). The average number of valves in the femoral vein between the inguinal ligament and the hiatus in adductor magnus is 3. These findings are in general agreement with those of Powell and Lynn.

Friedreich reported an incidence of 81 per cent for valves in the upper 5 centimeters of the femoral vein (i.e., approximately the segment above the saphenofemoral junction). Analysis of the results reported by Powell and Lynn and by Eger and Wagner reveals the incidence for such valves in their series to be approximately 72 and 67 per cent, respectively. In our present series the incidence is 67 per cent. Hesse and Schaak (7) reported in 1911 that 72 per cent of femoral veins in 100 limbs contained 1 valve above the mouth of its profunda tributary and another 5 per cent contained 2 valves. Taking all results and conditions into consideration it may be stated as fact that just over ⅔ of all femoral veins have a valve at the upper end and that almost all of these are within 1 centimeter of the inguinal ligament.

The region of the mouth of the profunda tributary.—Contrary to the early report of Friedreich, who stated that the femoral vein usually contains a valve just above the mouth of the profunda tributary, 89.5 per cent of our femoral veins had a valve just *below* the mouth of its profunda tributary. Powell and Lynn, working independently, found such a valve in 93 per cent. Kampmeier and Birch showed fairly conclusively that valves are most often seen in main veins distal to the mouths of tributaries. Thus, it may be stated with assurance that about 90 per cent of femoral veins contain a valve just below the junction with the profunda femoris tributary. Indeed, this is the most constant site for a valve in the main channel.

Segment of vein below the profunda tributary.—The findings in the present series indicate that about ⅔ of all femoral veins contains 2 or 3 valves below the level of the mouth of the profunda tributary, but that there is no pattern of bilateral symmetry. Occasionally there is no valve or there are as many as 5 valves along this part of the vein.

SUMMARY AND CONCLUSIONS

1. The presence or absence of valves in the main venous trunk above or proximal to the mouth of the long saphenous vein is, at most, only of theoretical importance in the etiology of saphenous varices.

2. In a series of 76 limbs, only 1 had long saphenous varices; another limb had varices in the proximal end of the short saphenous vein. In neither was there an absence of competent valves above the mouth of the vein involved.

3. Judging from the accumulated data of four independent studies involving many hundreds of veins, one in four external iliac veins (24 per cent) contains a valve. More

than ⅔ of these are competent. Valves in the common iliac vein are not as rare as it was believed formerly, but few, if any, are competent. Valves are not seen in the adult inferior vena cava.

4. Special note should be made of reports on the frequent occurrence of adhesions within the lumen of the common iliac vein. These are mostly on the left side, a fact that may account for the greater incidence of thrombosis on that side.

5. The femoral vein contains an average of 3 valves. Rarely, there may be none and, uncommonly, as many as 6. On macroscopic examination, almost all of the valves in the femoral vein appear to be competent.

6. The commonest site of a valve in the femoral vein is just distal to the mouth of the profunda tributary (about 90 per cent incidence). The second commonest site is at, or just distal to, the inguinal ligament, where over ⅔ of all femoral veins have a valve.

7. With few exceptions, the valves in the main venous trunk of the lower limb are bicuspid, having an anterior and a posterior cusp.

REFERENCES

1. Di Dio, L. J. A. Estudo anatômica de particularidades normais e patológicas da superfície interna da veia ilíaca comum esquerda. Thesis. Univ. of São Paulo, Brazil; Arq. cirug. clín. S. Paulo., 1949, 12: 507–616.
2. Idem. Valvulas das veias iliacus comuns em brancos, negros e mulatos. Rev. Hosp. clín., S. Paulo., 1951, 4: 343–359.
3. Eger, S. A., and Caspar, S. L. Etiology of varicose veins from anatomic aspect, based on dissection of 38 adult cadavers. J. Am. M. Ass., 1943, 123: 148–149.
4. Eger, S. A., and Wagner, F. B., Jr. Etiology of varicose veins. Postgrad. M., 1949, 6: 234–238.
5. Ehrich, W. E., and Krumbhaar, E. B. A frequent obstructive anomaly of the mouth of the left common iliac vein. Am. Heart J., 1943, 26: 737–750.
6. Friedreich, N. Ueber das Verhalten der Klappen in den Cruralvenen, sowie ueber das Verkommen von Klappen in den grossen Venanstaemmen des Unterleibes. Morph. Jahrb., 1882, 7: 323–325.
7. Hesse, E., and Schaak, W. Die Klappenverhaeltnisse der Oberschenkelvene und der Vena saphena magna in ihrer klinischen Bedeutung fuer die Operation der sapheno-femoralen Anastomose bei Varicen. Virchow's Arch., 1911, 205: 145–154.
8. Idem. Die anatomisch-physiologische und klinische Bewertung der sapheno-femoralen Anastomose bei Varicen, unter besonderer, Berueksichtigung der Dauerresultate dieser Operation. Beitr. klin. Chir., 1921, 124: 1–83.
9. Kampmeier, O. F., and Birch, C. La F. The origin and development of the venous valves, with particular reference to the saphenous district. Am. J. Anat., 1927, 38: 451–499.
10. Lynn, R. B. Personal communication.
11. McMurrich, J. P. The valves of the iliac vein. Brit. M. J., 1906, 2: 1699–1700.
12. Idem. The occurrence of congenital adhesions in the common iliac veins, and their relation to thrombosis of the femoral and iliac veins. Am. J. M. Sc., 1908, 135: 342–346.
13. Ochsner, A., and Mahorner, H. R. The modern treatment of varicose veins; with a review of 285 cases. Surgery, 1937, 2: 889–902.
14. Powell, T., and Lynn, R. B. The valves of the external iliac, femoral, and upper third of the popliteal veins. Surg. Gyn. Obst., 1951, 92: 453–455.

FURTHER STUDIES ON THE PATHOGENESIS OF COLD-INDUCED MUSCLE NECROSIS

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In another paper (8) degenerative changes in rabbit muscle were described which were manifested grossly and microscopically as early as 15 minutes after exposure of a leg to cold baths at −12 degrees C. for 30 minutes and which progressed to complete necrosis. The early degenerative changes were not observed in muscles rendered ischemic by the application of occlusive tourniquets to legs for periods up to 90 minutes. It was therefore concluded that they were due to the direct action of cold on the muscle cells—a true thermal injury.

The purpose of this investigation was to gain further knowledge concerning the nature of cold-induced muscle necrosis and to compare the degenerative changes with those caused by heat and ischemia.

METHODS

Male albino rabbits weighing more than 2,500 grams were used.

To compare cold-induced and heat-induced muscle degeneration, a hind leg of a number of animals was depilated, covered with a condom boot, and injured in the following manner: In some legs cold lesions were produced by exposure to an alcohol bath cooled with dry ice to temperatures of −10 degrees to −40 degrees C. for periods varying from 2 minutes 45 seconds to 30 minutes. In other legs burn lesions were produced under pentothal sodium anesthesia by immersion in a warm water bath at +42, +50, or +52 degrees C. for from 2 minutes to 3 hours. The animals were sacrificed 30 minutes to 23 days after injury and the tibialis anticus and extensor digitorum longus muscles, which make up a common muscle belly on the anterior aspect of the leg, were removed and fixed in formalin. Multiple longitudinal sections and, in some instances, cross sections were cut from the distal two-thirds of the muscle and stained with eosin and hematoxylin.

In order to compare ischemic muscle changes with those produced by cold, occlusive tourniquets were placed on the hind legs of anesthetized rabbits for periods of from 2 to 3½ hours and the animals sacrificed after various time intervals ranging from 30 minutes to 1 week. Histologic sections were prepared as described from the distal two-thirds of the tibialis anticus and extensor digitorum longus.

To determine whether ice-crystal formation was essential for the production of cold-induced muscle necrosis several animals had a hind leg prepared as described previously and immersed in an alcohol bath at +1 degree C. for periods of from 16 to 60 hours. The animals were sacrificed after varying time intervals up to 3 days, and histologic sections were made of the common belly of the tibialis anticus and extensor digitorum longus.

RESULTS

Gross findings. Muscles exposed to a degree of heat or cold injury which, according to our experience, ultimately resulted in macroscopic necrosis showed gross abnormalities immediately after exposure to heat and as early as 15 minutes after thawing of the frozen legs. They were swollen, bluish in color, less translucent, and more friable than normal. The swelling decreased after 3 to 4 days and well demarcated gross necrosis was visible after 72 hours. The skin of the leg did not become necrotic in the cold-injured animals but generally did in those injured with heat.

Macroscopic changes were not apparent 30 minutes after the release of occlusive tourniquets applied for a period of time (3½ hours) which ordinarily resulted in scattered areas of gross muscle necrosis at the end of 1 week. Even after 24 hours gross changes were mini-

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mal and consisted of slight swelling and paleness. At the end of 48 hours small areas of hemorrhage in the muscles were observed. In our experience gross necrosis of muscle did not occur as early as 72 hours after complete ischemia for a period of 3 hours but was apparent at the end of 7 days. Skin necrosis rarely occurred.

Microscopic findings. In muscles exposed to a degree of cold injury (−40 degrees C. for from 2 to 3 mins.) that resulted in acute cell death of only the superficial layers of the tibialis anticus, i.e., those closest to the alcohol bath, three definite histologic lesions, each at a different depth, were identified. The most severe of these was represented as a narrow shell of coagulation necrosis involving the superficial muscle layers closest to the exposure bath. Just beneath this zone and sharply differentiated from it was a second layer of lesser injury—slow muscle necrosis with extensive fibrosis. Still deeper and involving an area paralleling the other two was a third zone of least injury, that of simple atrophy, which bordered normal appearing muscle on its deep margin (Fig. 1). The line of demarcation between the zones of slow necrosis and atrophy was not sharp, indicating a slow transition from one to the other.

These same three histologic lesions were produced in the corresponding muscle areas of other animals by heat (+52 degrees C. for 3 mins.) (Fig. 2) and by the application of occlusive tourniquets for relatively long periods (2 to 3½ hr.) (Fig. 3). The heat-induced muscle lesions were layered in the same manner as those produced by cold. However, in the cases of ischemic degeneration, the three types of lesions were not layered from the surface of the muscle. It was necessary to apply the occlusive tourniquets for periods of time which were critical for muscle survival (usually 2 to 3½ hours) in order to produce adjacent areas of coagulation necrosis, slow necrosis, and atrophy which were distributed at random throughout the muscle.

In the case of cold or heat injury it was possible to allow the surface muscle layers to escape coagulation necrosis by using a less severe exposure so that slow necrosis then appeared on the surface. By using a still less severe exposure, the superficial layers showed only atrophy.

Coagulation necrosis. These changes were described in another paper (8) with regard to cold injury and began as early as 15 minutes following exposure. Figure 7 shows the acute muscle cell degeneration in the tibialis anticus 30 minutes after exposure. Even this early, segments of many fibers showed vacuolation and fenestration or were broken up into irregular masses with or without destruction of the sarcolemma. Other fibers retained their form. In the cells that showed degeneration the nuclei exhibited little or no change. Identical histologic changes were present 15 and 30 minutes after exposure to heat (Fig. 8). Thirty minutes and 1 hour after the release of tourniquets applied for 3½ hours a few muscle fibers exhibited these same changes but they were not numerous until after 2 hours (Fig. 9).

The changes described progressed to complete necrosis within a few days in all three types of injury. The necrotic muscle cells were swollen, showed disintegration with loss of nuclei, stained bright pink with eosin, tended to be hyaline, and often were broken up into amorphous clumps. Some fibers were vacuolated; others were ruptured and contracted in segments with the formation of clots or caps at the margins of the defect. The space between the ruptured ends was either empty or contained pink granular or honeycombed material with or without an intact sarcolemma. In some the cross striations were absent but just as often they appeared normal or were more prominent than usual with or without separation into discs at the striations. This latter observation has been called "discoid fragmentation" by Kopits. In the most severely injured areas many fibers were not broken up but maintained their form for days. These fibers were swollen and hyalinized. In some such fibers the cross striations were either completely absent or missing in certain segments. Others showed normal or even more than normally prominent striations.

Cellular activity was lacking or minimal in the center of the necrotic areas but was pronounced at the margins. In these peripheral

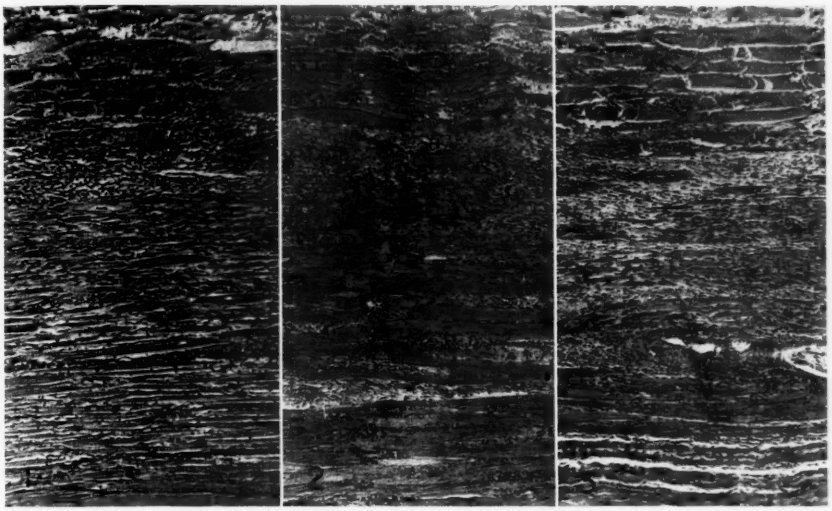

Fig. 1. Tibialis anticus from leg exposed to a bath at −40 degrees C. until temperature in superficial layers of muscle reached −10 degrees C. (2 min. 45 sec.) and then immediately rewarmed in water at 42 degrees C. Survival time, 7 days. Hematoxylin and eosin stain. ×51. Three histologic lesions are present in three zones which are layered from the cutaneous surface of the muscle in the following order: (1) coagulation necrosis, (2) slow necrosis with fibrosis, and (3) atrophy.

Fig. 2. Tibialis anticus from leg exposed to a bath at +52 degrees C. for 3 minutes. Survival time, 7 days. Hematoxylin and eosin stain. ×51. The same three histologic lesions, occupying the same layered zones as in Figure 1, are present.

Fig. 3. Deep area of tibialis anticus from leg rendered ischemic for 3½ hours by occlusive tourniquet. Survival time, 7 days. Hematoxylin and eosin stain. ×51. The same three histologic lesions as in Figures 1 and 2 are present in layers but do not bear the same relationship to the muscle surface.

areas phagocytes were numerous and active in removing the dead muscle. There were a few polymorphs and lymphocytes. In some instances the sarcolemmic sheaths were filled with large mononuclear phagocytes. Fibroblastic proliferation with mitoses was present in these areas. Small hemorrhages were commonly observed (Figs. 10, 11, 12).

It should be mentioned that not uncommonly isolated fibers in the muscles of the unexposed leg, for reasons which are obscure, showed the same contracture lesions as the muscles of the exposed leg.

Coagulation necrosis with breaking up of muscle fibers, identical histologically with that observed in frozen and subsequently thawed muscle, was produced by immersing legs in baths at a temperature above freezing (+1 degree C.) for relatively long periods of time (16 to 60 hours) (Fig. 21).

Slow necrosis. This lesion represented a slightly lesser degree of injury than coagulation necrosis. At the end of a week the muscle cells showing this injury were greatly reduced in size and stained poorly with eosin. Many fibers had disappeared and only remnants of others remained in the midst of extensive fibrosis. The remaining portions of fibers showed longitudinal splitting and often hypernucleation. Sometimes as many as 30 or 40 nuclei were present in a single fiber lined up side by side or overlapping either in the center of the cells or, less often, beneath the surface. The nuclei were enlarged, pale, round or oval, and often contained prominent nucleoli. Mitoses were not seen. The sarcolemmic nuclei also were enlarged and more numerous than normal in areas. Surrounding the masses of nuclei were pale, clear, or granular zones in the sarcoplasm which often tapered for considerable distances toward the ends of the muscle fibers. Cross striations were faint but often could be made out in very severely degenerated cells.

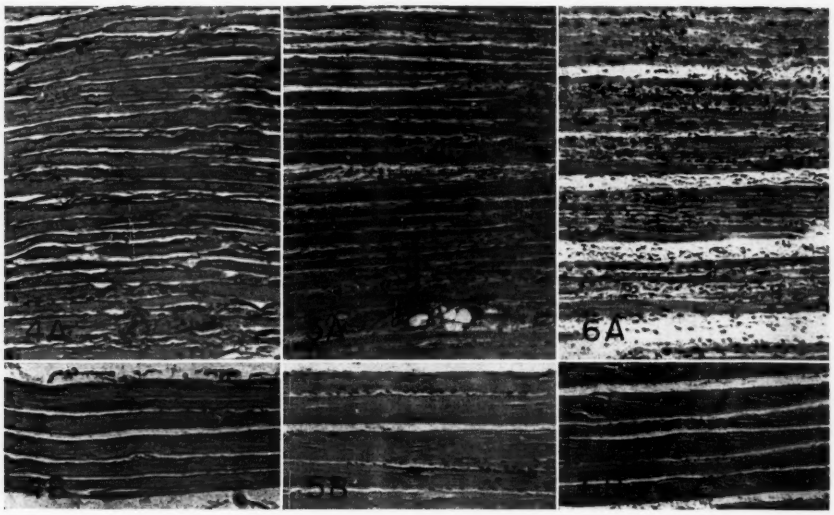

Fig. 4. A, Tibialis anticus from leg exposed to a bath at −10 degrees C. for 30 minutes. Survival time, 19 days. Hematoxylin and eosin stain. ×68. Muscle fibers are decreased in size but with rare exceptions maintain their form. B, Normal tibialis anticus from unexposed leg of same animal as Fig. 4A. Hematoxylin and eosin stain. ×68.

Fig. 5. A, Tibialis anticus of leg exposed to a bath at +42 degrees C. for 3 hours. Survival time, 7 days. Hematoxylin and eosin stain. ×68. Muscle fibers are decreased in size but maintain their form. B, Normal tibialis anticus from unexposed leg of same animal as in Figure 5A. Hematoxylin and eosin stain. ×68.

Fig. 6. A, Extensor digitorum longus from a leg rendered ischemic by occlusive tourniquet for 2½ hours. Survival time, 7 days. Hematoxylin and eosin stain. ×68. Muscle fibers much reduced in size and have largely but not entirely maintained their form. The changes in some fibers have gone beyond simple atrophy and represent early slow necrosis. B, Extensor digitorum longus from normal leg of same animal as in Figure 6A. Hematoxylin and eosin stain. ×68.

Fibroblastic proliferation with many mitoses was prominent in this zone, replacing the slowly degenerating muscle cells. Inflammatory cells were absent except for an occasional lymphocyte. Macrophages were not observed (Figs. 13, 14, 15).

In some muscle areas showing the slow type of necrosis and very rarely in muscles displaying coagulation necrosis, whether produced by cold, heat, or ischemia, giant cell formation was a prominent feature. These muscle giant cells tended to occur in clumps and formed from masses of degenerating sarcoplasm within which were numerous large nuclei (Fig. 20). These cells enlarged with age and ultimately their centers degenerated into granular debris which in some instances stained basophilic suggesting calcium deposition. In these latter cells the nuclei were pushed to the periphery and eventually disappeared. Connective tissue proliferation was more pronounced in the giant cell areas, forming expanding masses which tended to push away adjacent muscle fibers (Figs. 16, 17, 18). When located near the muscle surface the latter was rendered irregular by the proliferating tissue.

Ringbinden as described by Wohlfahrt and Wohlfahrt were demonstrable in cross sections of muscle areas, the seat of long-standing slow degeneration, and were characterized by cylindrical or C shaped masses of muscle fiber material surrounding a central core (Fig. 19).

Atrophy. This change was observed within a few days after exposure. Cells showing this least severe injury maintained their form but were reduced in size. Hypernucleation of the sarcolemma and of some muscle fibers was present in this area, but the majority of the

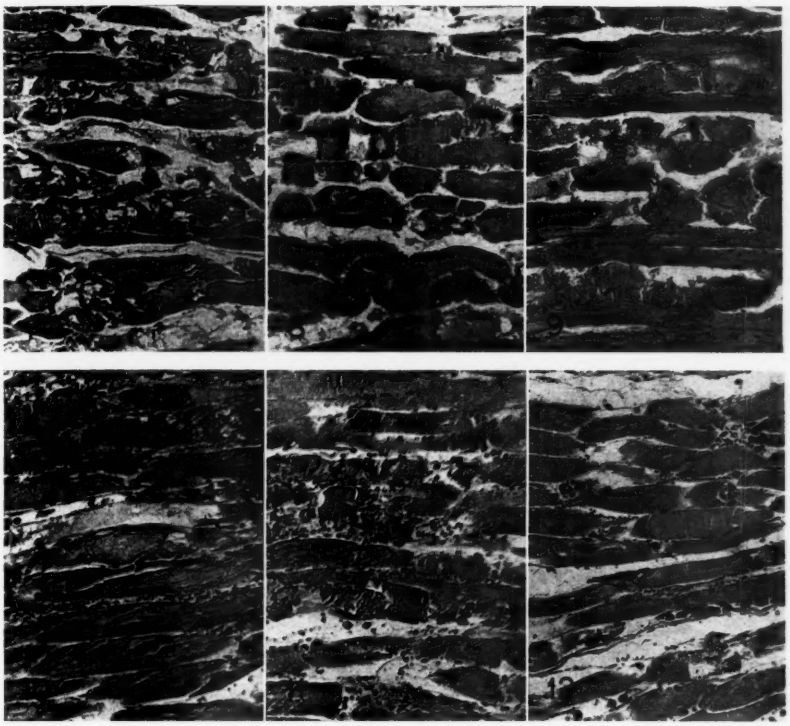

Fig. 7. Tibialis anticus from leg exposed to a bath at −12 degrees C. for 30 minutes. Survival time, 30 minutes. Hematoxylin and eosin stain. ×68. Extensive degeneration of muscle fibers.

Fig. 8. Tibialis anticus from leg exposed to a bath at +50 degrees C. for 20 minutes. Survival time, 30 minutes. Hematoxylin and eosin stain. ×68. Some muscle fibers show the same degeneration as in Figure 7.

Fig. 9. Tibialis anticus from leg rendered ischemic by occlusive tourniquet for 3½ hours. Survival time, 2 hours. Hematoxylin and eosin stain. ×68. Muscle fibers show the same changes as in Figures 7 and 8.

Fig. 10. Superficial portion of tibialis anticus from leg exposed to a bath at −40 degrees C. for 2 minutes and 45 seconds. Survival time, 7 days. Hematoxylin and eosin stain. ×102. (Same slide as Fig. 1.) Muscle fibers are swollen and tend to be hyaline; some show fragmentation. Cells other than muscle are mostly macrophages with some extravasated erythrocytes and a few proliferating fibroblasts.

Fig. 11. Superficial portion of tibialis anticus from leg exposed to a bath at +52 degrees C. for 3 minutes. Survival time, 3 days. Hematoxylin and eosin stain. ×102. Same changes as in Figure 10.

Fig. 12. Deep portion of tibialis anticus from leg rendered ischemic for 2 hours by occlusive tourniquet. Survival time, 7 days. Hematoxylin and eosin stain. ×102. Same changes as in Figures 10 and 11.

cells presented the picture of simple atrophy especially in the deep fibers as one approached the normal muscle in cases of injury by heat or cold (Figs. 4, 5, 6).

DISCUSSION

Histologic observations made in muscle of rabbit legs following local exposure to cold alcohol baths indicate that there are successive degenerative lesions and that the final degree of injury depends on the degree of cold exposure. Three distinguishable lesions were observed, representing three consecutive degrees of cold injury. These are, in the order of decreasing severity, (1) coagulation necrosis, (2) slow necrosis, and (3) atrophy. By using

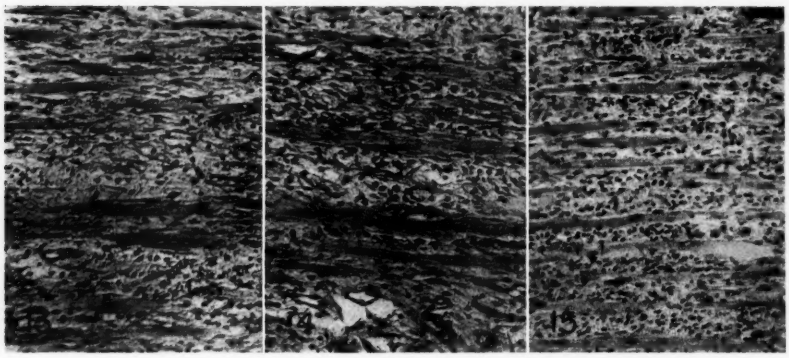

Fig. 13. Area of tibialis anticus just beneath superficial zone of coagulation necrosis. Leg exposed to a bath at −40 degrees C. for 2 minutes and 45 seconds. Survival time, 7 days. Hematoxylin and eosin stain. ×102. (Same slide as Figs. 1 and 10.) Muscle cells much reduced in size and degenerated. Many have disappeared. Hypernucleation of some remaining segments of muscle cells. Advanced fibrous replacement.

Fig. 14. Area of tibialis anticus just beneath superficial zone of coagulation necrosis. Leg exposed to a bath at +52 degrees C. for 4 minutes. Survival time, 7 days. Hematoxylin and eosin stain. ×102. Same changes as in Figure 13.

Fig. 15. Deep portion of extensor digitorum longus. Leg rendered ischemic for 3 hours by occlusive tourniquet. Survival time, 7 days. Hematoxylin and eosin stain. ×102. Same changes as in Figures 13 and 14.

the proper degree of cold exposure all three lesions can be produced in the same muscle which are layered so that the most severe (coagulation necrosis) is nearest to, and the least severe (atrophy) is farthest from, the cold bath. Slow necrosis is observed in a layer between these two. This layering of the lesions from the surface according to severity cannot logically be explained on a vascular basis. Certainly they do not represent the picture of an infarct.

Coagulation necrosis is an acute phenomenon. Some, but not all changes observed, are undoubtedly due to contracture of muscle fiber segments the strength of which exceeds the tensile strength of the injured fibers. They appear to be the same as those described by Speidel in muscle fibers of several animal species after electrical stimulation, by Wiercinski and Cookson after injection of trypsin into the cut ends of muscle fibers, and by Godeaux as well as Nageotte after thawing of frozen isolated muscle fibers. These phenomena are most numerous after cold exposures which are critical for the development of coagulation necrosis (−12 degrees C. for 30 mins. in our experiments) and indicate that a particular state of muscle excitability is necessary for the maximum production of the lesions. With this degree of cold injury most of the contracture lesions are located at the margin of the necrotic zone and even involve single or small groups of fibers deeper in the apparently normal muscle. Exposure of a leg to a bath at −70 degrees C. for 30 minutes, a degree of exposure which results in complete gangrene in 100 per cent of animals, produces relatively few contracture phenomena even after 4 hours. This observation tends to confirm the idea that the state of muscle excitability is important for the production of contracture lesions.

The dead cells tend to become hyaline with or without loss of cross striations in a few hours and compare favorably with the description of Zenker's hyaline degeneration as occurs in striated muscles in cases of typhoid fever. Similar changes in muscle have been reported by Forbus (3) in pneumonia patients, by Cohnheim in experimentally produced ischemia in frog tongues, and by Forbus (4) in experimental muscle necrosis produced by local injection of phenol, boiling water, alcohol, or by application of tourniquets.

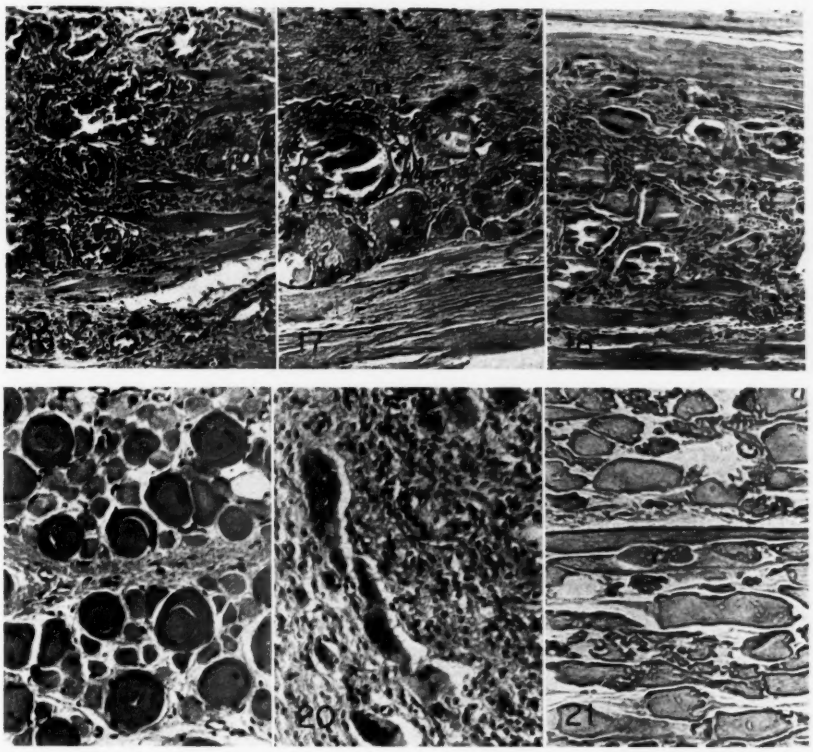

Fig. 16. Area of slow necrosis in tibialis anticus. Leg exposed to a bath at −36 degrees C. for 3 minutes 10 seconds. Survival time, 7 days. Hematoxylin and eosin stain. ×85. Large muscle multinucleated giant cells. Some show central degeneration with nuclei at the cell periphery. Considerable intercellular fibrosis.

Fig. 17. Area of slow necrosis in tibialis anticus. Leg exposed to a bath at +50 degrees C. for 2 minutes and 10 seconds. Survival time, 7 days. Hematoxylin and eosin stain. ×136. Same changes as in Figure 16.

Fig. 18. Area of slow necrosis in deep portion of tibialis anticus. Leg rendered ischemic for 2 hours by occlusive tourniquet. Survival time, 7 days. Hematoxylin and eosin stain. ×85. Same changes as in Figures 16 and 17.

Fig. 19. Cross section of muscle in margin of necrotic area from leg exposed to a bath at −15 degrees C. for 30 minutes. Survival time, 23 days. Hematoxylin and eosin stain. ×143. Several *Ringbinden* are present in area of muscle degeneration.

Fig. 20. Same slide as Figure 19 but from healing area of coagulation necrosis. ×143. Multinucleated giant cells have formed from necrotic portions of muscle cells. Extensive fibrous replacement.

Fig. 21. Extensor digitorum longus of leg exposed to a bath at +1 degree C. for 16 hours. Animal expired at end of 16 hour immersion period. Hematoxylin and eosin stain. ×68. Almost all muscle fibers have broken up into amorphous masses. Most fibers show loss of cross striations, are swollen, and stain poorly with eosin.

Forbus suggested that in the pneumonia cases reported by him bacterial toxins probably caused the muscle necrosis. It is possible that high fever for a sufficient length of time was a factor since the same changes can be produced by artificially raising the muscle temperature with warm water baths. Malamud and associates have described comparable lesions involving heart muscle in cases of heat stroke.

In cold-induced necrosis, healing occurs by scar formation in contrast to muscle regenera-

tion without scarring as described by Forbus in cases of muscle injury in typhoid and pneumonia.

Except for the contracture phenomena early changes in acute cell death are few and not striking. This emphasizes the limitation of histologic examination to determine early changes that are undoubtedly chemical in nature. The state of the cross striations is not a true index of the degree of cell damage.

One can only speculate as to the cell changes produced by cold which result in acute cell death. It is important to point out that neither freezing followed by thawing (Nageotte; Godeaux) nor ice-crystal formation (Lewis and Love; Blackwood) are essential for the production of acute necrosis since they also result from relatively long exposure to bath temperatures above o degree C. We can only say that cellular changes are produced in muscle by cold which may result in either acute or slow cell death or atrophy.

The second and less severe type of necrosis requires more time to develop, but ultimately results in cell death and fibrous replacement. It has been called degenerative atrophy (Kopits and Tower) in contrast to simple atrophy in which the cell morphology is preserved. Tower has described this lesion as well as simple atrophy in denervated cat muscle and pointed out that they represent consecutive changes.

The hypernucleation of degenerating muscle cells appears to be a futile attempt on the part of the dying fibers to regenerate. There is disagreement among writers on this subject as to whether the observed hypernucleation represents an actual increase in the number of nuclei or whether they are due to migration and condensation of pre-existing nuclei in a reduced mass of myoplasm. We agree with Tower that it is very difficult to conclude from the observations that the increase in the number of nuclei is not real.

The confinement of the least severe lesion, i.e., simple atrophy, to a zone paralleling the exposed muscle surface and lying between the areas of slow necrosis and normal appearing muscle and the rapidity of its development suggest that the atrophy is due to the direct effects of cold. This peculiar distribution of the lesion does not support the idea that the atrophy is due to disuse of the leg or to nerve injury. Furthermore, our ability to produce at will the zone of atrophy at the muscle surface adjacent to the bath by using a less severe exposure than required to produce coagulation or the slow type necrosis also favors the hypothesis that the lesion is a result of direct cold injury.

The meaning of giant cell formation in some muscle areas, especially those undergoing slow necrosis, is not apparent.

The significance of *Ringbinden* has not been clarified. Wohlfahrt and Wohlfahrt mentioned their occurrence in progressive muscular dystrophy, dystrophy myotonica, Basedow's disease, as well as in ocular muscles under normal conditions. They are said to represent spiral masses of muscle fibrils just beneath the sarcolemma and enclose the central mass of the muscle fiber containing longitudinal fibrils.

Even though the same lesions can be produced by cold, heat, or tourniquets, the application time required of each to produce these injuries is not the same. Cold is less efficient than heat but more efficient than ischemia as a means of producing muscle necrosis. Cells may be killed instantaneously with heat but ischemia requires at least 2 hours, in our experience, and sometimes longer to produce coagulation necrosis of muscle. The time required by cold to produce like changes lies somewhere between these two extremes. The fact that coagulation necrosis can be produced by shorter exposures to heat and cold than to ischemia from tourniquets indicates that in the former instances the injury is a direct one on the cells rather than being secondary to vascular injury. Furthermore, the similarity of the cold-produced muscle changes and the heat-produced lesions adds support to the idea that the former are true thermal injuries.

Each of these three injury-producing agents must produce cellular metabolic abnormalities, not necessarily identical, which result in lesions varying in severity from simple atrophy to coagulation necrosis. The nature of these processes is unknown at present and it will remain for the chemist to discover the mech-

anism of cell death. Careful consideration should be given to enzyme systems and also to the denaturization and dehydration of proteins.

Harkins has described the similarity of certain vascular changes in frostbite and burns. The similarity of the clinical picture in both humans and experimental animals should be obvious to all who have observed burn and cold injuries.

SUMMARY AND CONCLUSIONS

Cold, heat, and ischemia produce the same pathologic changes in muscle, but the application time required for each to produce like changes is different. Heat requires the least time and ischemia the greatest, with cold occupying a time of action between those two.

Three distinct histologic lesions, representing different degrees of injury which are consecutive, can be observed in injuries induced by cold, heat, or ischemia. In the cases of controlled heat and cold injuries the three lesions are layered from the muscle surface closest to the exposure bath in the order of decreasing severity as follows: (1) coagulation necrosis, (2) slow necrosis, and (3) atrophy. In controlled ischemic injuries produced by the application of occlusive tourniquets the three lesions are not layered from the surface but are scattered at random throughout the muscle.

Especially in the margins of areas of coagulation necrosis, many fibers show phenomena which appear to be secondary to contracture of injured muscle fibers and are characterized by fragmentation of segments of the sarcoplasm. A definite state of excitability appears to be necessary for the maximum production of these changes.

Ice-crystal formation is not essential for the production of coagulation necrosis or the contracture phenomena in local cold injury since both occur after exposure to baths at temperatures above freezing for relatively long periods of time.

The gross and microscopic changes in muscle are identical whether produced by heat or cold. This indicates that the two agents act in the same manner to produce the lesions, and it is generally admitted that heat produces a true thermal injury. Evidence that cold-induced injuries are not secondary to ischemia from vascular thrombosis is obtained in the observation that, to produce the same lesions, tourniquets had to be applied for much longer periods of time than was necessary with cold.

Cold must produce metabolic cellular changes which in relatively mild exposures results in disturbed metabolism leading to atrophy, and in more severe exposures leads to cell death either acutely (coagulation necrosis) or more slowly (slow necrosis).

REFERENCES

1. Blackwood, W. Injury from exposure to low temperature; pathology. Brit. M. Bull., 1944, 2: 138–141.
2. Cohnheim, J. F. Untersuchungen ueber embolische Prozesse. Berlin: A. Hirschwald, 1872. Quoted by Speidel (12).
3. Forbus, W. D. Pathologic changes in voluntary muscles—I, degeneration and regeneration of the rectus abdominis in pneumonia. Arch. Path. Lab. Med., 1926, 2: 318–339.
4. Idem. Pathologic changes in voluntary muscle—II, experimental study of degeneration and regeneration of striated muscle with vital stains. Arch. Path. Lab. Med., 1926, 2: 486–499.
5. Godeaux, J. Considérations sur la contracture de décongélation du muscle strié de grenouille. Arch. internat. physiol., Liége., 1950, 58: 299–312.
6. Harkins, H. N. The Treatment of Burns. Springfield, Ill.: Charles C Thomas, 1942.
7. Kopits, K. Beitraege zur Muskelpathologie. Arch. orthop. Unfallchir., 1929, 27: 277–403.
8. Lewis, R. B. Pathogenesis of muscle necrosis due to experimental local cold injury. Am. J. M. Sc., 1951, 222: 300–307.
9. Lewis, T., and Love, W. S. Vascular reactions of the skin to injury—III, some effects of freezing, of cooling, and of warming. Heart, Lond., 1926, 13: 27–60.
10. Malamud, N., Haymaker, W., and Custer, R. P. Heat stroke; a clinicopathologic study of 125 fatal cases. Mil. Surgeon, 1946, 99: 397–449.
11. Nageotte, J. Sur la contraction extrême des muscles squellettiques chez les vertébrés. Zschr. Zellforsch., 1937, 26: 603–624.
12. Speidel, C. C. Studies of living muscles—II, histological changes in single fibers of striated muscle during contraction and clotting. Am. J. Anat., 1939, 65: 471–529.
13. Tower, S. S. The reaction of muscle to denervation. Physiol. Rev., 1939, 19: 1–48.
14. Wiercinski, F. J., and Cookson, B. A. Action of dilute trypsin on muscle protoplasm (motion picture). Fed. Proc., Balt., 1949, 8: 165.
15. Wohlfahrt, S., and Wohlfahrt, G. Mikroskopische Untersuchungen an progressiven Muskelatrophien. Acta med. scand., 1939, Suppl. 63: 1–137.
16. Zenker, F. A. Ueber die Veraenderungen der willkuerlichen Muskeln im Typhus abdominalis. Leipzig: F. C. W. Vogel, 1864. Quoted by Speidel (12).

TREATMENT OF CARCINOMA OF THE CERVIX UTERI

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IN the Gynecological Department of the Okayama University Hospital, cancer of the cervix uteri is treated by two methods: radiation therapy with x-ray and radium, as is widely applied in many countries, and Okabayashi's operation with postoperative radiation. This radical operation is now regarded in Japan as the standard operation for the disease but is still unknown in other countries.

All cases are classified into four stages by the rule of the 1929 International Classification of the League of Nations' Committee.

Radiation therapy is applied to stage III except for the few cases treated by operation and to all stage IV cases, while in stages I and II, operation or radiation is chosen freely by the patient and the family. Thus the two groups—operation and radiation—are available for evaluation in stages I and II, which consist of unselected cases. The results of treatment after 5 years may permit a comparison of the two groups to enable us to discover the salvage rate by this type of operation, and whether an operative approach can be approved in spite of the recent progress of radiation therapy.

MATERIALS AND METHODS OF TREATMENT

In the 10 year period from 1935 to 1945, a total of 1,101 patients with cancer of the cervix uteri were examined and admitted into the hospital. Complete treatment was given to 1,062 while 39 patients were incompletely treated or refused treatment. The specimens were verified as cancer histologically. The microscopic groups are tabulated according to Crossen (Table I). Carcinoma in situ or preinvasive cancer (stage 0) was excluded.

The histological classification was of little value in the determination of the outcome of the therapy. It was found that the extent of the disease, not the cell type, was important.

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The percentage of each stage can be seen in Table II, showing the relative position of the present status of cancer patients in Japan. Stages III and IV occupy almost one half of the total cases. Methods of treatment employed are elucidated in Table III.

All the cases were pursued in the follow-up examination during 5 consecutive years until 1950. Nine cases (0.82 per cent) were lost sight of in the radiation group, while all were followed in the operation group.

RADIATION THERAPY

Apparatus. The x-rays are delivered from deep x-ray machines using 160 kilovolts, 2 to 2.5 milliamperes, a target skin distance of 30 centimeters, a field area 8 by 8 centimeters, filters 0.5 millimeter of copper plus 1.0 millimeter of aluminum, and a half-value layer equal to 0.8 millimeter of copper. The radium dose available for the treatment is 248 milligrams, of which Dominici tubes are 7 and radium cells 29.

Technique of radiation. The treatment is started with deep radiation followed by radium application constituting the first series. After an interval of 2 months the second series of deep radiation without radium is applied. The deep roentgen radiation consists of a "simple fractional method," but not "protracted" as was done by Coutard, radiating 300 roentgens every day on one field. Four fields are laid, 2 ventral and 2 dorsal, on the lower abdomen. Each field is repeated 3 times so that a total of 3,600 roentgens is given over 12 days. This method is applied equally to all stages.

Roentgen therapy is followed by radium, which is applied in different dosage according to the stage. However, on an average, 5,000 to 8,000 milligram hours are given for stages I and II, and 10,000 to 12,000 milligram hours for stages III and IV. A dosage of 700 to 1,200 milligram hours is applied at one time, and is repeated on alternate days until the

TABLE I.—MICROSCOPIC CLASSIFICATION OF TUMORS

	Total No.	Per cent
1. Squamous cell carcinoma		
Grade I	86	7.8
Grade II	793	72.1
Grade III	191	17.3
2. Adenocarcinoma	30	2.7
3. 1. and 2. combined	1	0.1

tal dose is given. One third or one fifth of the total dosage is applied in the cervical canal.

Two months after the first treatment, the second series is begun. Deep radiation is applied equally to all stages as in the first series, but, with the addition of another field at the vulva, so that 15 fields are radiated for the total of 4,500 roentgens. The total dose administered in the two series amounts to 8,100 roentgens.

The group treated in this manner comprised 3 cases (method A).

The second group is a combination of deep roentgen radiation and Schaefer's intravaginal cone radiation in place of radium (method B, 4 cases). The dose of the intravaginal application varies according to the size of the tumor and the infiltration of parametria. The superficial dose is 1,000 roentgens at one field. Total dose given to the cervix and to both parametria on an average is 6,000 to 17,000 roentgens.

The third group is a combination of three procedures, deep roentgen radiation, radium, and Schaefer's cone (method C), and numbers 303 cases. The intravaginal radiation is usually given at the end, i.e., first deep x-ray followed by radium and then cone radiation, but sometimes it is given alternately with radium during the same period. In all cases the deep x-rays are applied as the first procedure. No cauterization should be done at all. Even in case of severe hemorrhage a tight tamponade is inserted to arrest it while the radiation is continued without interruption. Primary mortality of the radiation therapy was 2.46 per cent (17 in 689 cases).

TABLE III.—METHODS OF TREATMENT EMPLOYED (1935 to 1945)

	No.
Radiation therapy	689
A. X-ray and radium	343
B. X-ray and intravaginal cone	43
C. X-ray, radium, and intravaginal cone	303
Operation with postoperative radiation	373
A. Okabayashi	333
B. Abdominal hysterectomy	40

For the second and third groups, the second series is done in the same manner as the first group, as mentioned previously.

The patient is examined 2 months after the completion of these treatments. When the clinical course is favorable, the follow-up examination is repeated at intervals of 3 or 4 months, later 6 months, until the final examination is made at the sixth year. When the disease is not completely cured, or if a recurrence is recognized, the third series of the deep radiation is applied, as a further procedure.

OPERATIVE THERAPY

Two methods of operation, abdominal total hysterectomy and the Okabayashi operation were employed during this period (1935 to 1945). The former I call "simple total hysterectomy" in contrast to the latter, which is an "extensive total" one. Forty patients were operated upon by a simple total hysterectomy and 33 fell into stage I. The extirpated specimen consists of uterus with its adnexa and does not include the parametrial tissue. The results of this operation were shown not to surpass those of radiation therapy of the same stage, as elucidated in Tables IX and VI. Thus it has been abandoned in favor of the Okabayashi procedure in all operative cases.

The Okabayashi operation was first described in 1921 by Professor H. Okabayashi

TABLE II.—NUMBER OF PATIENTS TREATED IN EACH STAGE

Stage	No.	Per cent
I	107	9.7
II	488	44.3
III	398	36.2
IV	108	9.8
Total	1,101	

TABLE IV.—ABSOLUTE CURE RATE

Stage	No. of cases	Survival after 5 years without recurrence	Per cent
I	107	74	69.2
II	488	268	54.9
III	398	134	33.7
IV	108	13	12.0
Total	1,101	489	44.4

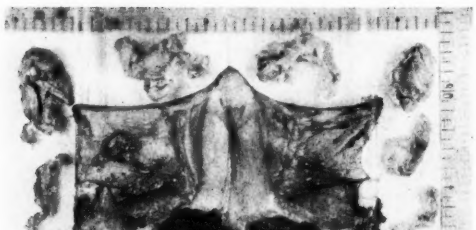

Fig. 1. Specimen of squamous cell carcinoma of the cervix, extirpated by the Okabayashi operation. Cauterization of the cervix was done directly before operation. The specimen shows uterus, adnexa, parametrial and paravaginal connective tissues, broadly dissected, and pelvic lymph nodes.

(5). It is a far more extensive hysterectomy than Wertheim's procedure. The main features of the technique consist of: (1) abdominal hysterectomy with the vaginal fornices, (2) systematic removal of the parametrial tissues as close as possible to the pelvic wall (considered more extensive than the Wertheim's method), and (3) systematic complete removal of all the pelvic lymph nodes. In that paper he advised excision of only enlarged glands, but in his second report in 1928 he recommended dissection of all lymph nodes, whether large or small, with lymph tracts in blocks, even in cases of an incipient cancer of stage I. The iliac, the hypogastric, the obturator, the inguinal, the sacral and the parametrial nodes are removed together with surrounding fat so as to bare the pelvic walls. This is the most important point in obtaining permanent cure. Recently Meigs also reported on the bilateral dissection of pelvic lymph nodes together with radical hysterectomy in 85 cases. Thus, the specimen extirpated by the Okabayashi method consists of parametrial and paravaginal connective tissues broadly attached to the cervix and the upper part of the vagina, and bilateral lymphatic nodes, large and small altogether, as shown in Figures 1 and 2.

TABLE V.—ABSOLUTE CURE RATE EXCLUDING 39 INCOMPLETELY TREATED CASES

Stage	No. of cases	Survival after 5 years without recurrence	Per cent
I	106	74	69.8
II	478	268	56.1
III	385	134	34.8
IV	93	13	14.0
Total	1,062	489	46.0

TABLE VI.—RELATIVE CURE RATE OF TOTAL RADIATION CASES

Stage	No. of cases	Survival	Per cent
I	40	23	57.5
II	216	109	50.5
III	340	114	33.5
IV	93	13	14.0
Total	689	259	37.6

Care before the operation. Operation is indicated in the patient with stages I, II, or III cancer, who is under 60 years of age and voluntarily agrees to operative treatment. The physical condition is minutely examined by routine diagnostic methods. Special attention is paid to the cardiac function which is tested by Kaufmann's diuresis method, Bickenbach's standing method, and electrocardiogram within 1 week, during which digitalis is administered routinely every day in small doses (the sum amounts to 1.5 to 2.0 gm.). Vaginal douche is performed with a solution of sulfonamides or antibiotics. If there is no contraindication, the operation is performed.

Care directly after the operation. An indwelling catheter is placed in the bladder for a period of about 10 days. Sulfonamides and antibiotics are administered daily in a planned manner.

Postoperative radiation. The therapy is applied from the third week after operation in all cases as a prophylaxis against recurrence. The dosage of deep roentgen radiation is the same as in the first series of the radiation

TABLE VII.—CURE IN THREE METHODS OF RADIATION

Stage	Method A			Method B			Method C		
	No.	Survival	Per cent	No.	Survival	Per cent	No.	Survival	Per cent
I	30	16	53.3	5	2	40.0	5	5	100.0
II	105	51	48.6	13	4	30.8	98	54	55.1
III	151	47	31.1	13	3	23.0	176	64	36.4
IV	57	8	14.0	12	0	0	24	5	20.8
Total	343	122	35.6	43	9	20.9	303	128	42.2

group, 300 roentgens a day and repeated 3 times over each of 4 fields for a total of 3,600 roentgens.

Complications of operation. Primary mortality of 7.2 per cent during this period includes death immediately after operation and during postoperative convalescence in the hospital. Ureterovaginal fistulas occurred in 3 per cent, one half of which were cured by roentgen castration of the kidney, while the rest healed spontaneously. Pelvic retroperitoneal abscess occurred in 7.42 per cent, which was cured by vaginal drainage and irrigation within 1 to 2 weeks.

RESULTS OF TREATMENT AND DISCUSSION

Absolute cure rate. All cases, radiological and operative, including 39 cases incompletely treated, are taken into account and an absolute cure rate after 5 years is calculated in Table IV.

The absolute cure rate is 44.4 per cent. If the 39 cases are excluded from study, the rate becomes 46.0 per cent (Table V).

Relative cure rate. Radiological cases.—The relative cure rate of the radiological treatment is 37.6 per cent as shown in Table VI. Relative cure rate differs according to the method of radiation therapy employed. The best result is obtained when method C—deep radiation, radium, and Schaefer's radiation—was employed, as indicated by 42.2 per cent relative 5 year cure rate; while method A—deep radiation and radium—revealed 35.6 per cent and method B—deep radiation and Schaefer's radiation—20.9 per cent (Table VII). This result indicates to us that in the radiological treatment large amounts of the radiation energy should be given during the first series. The difference in the result is believed to depend on the variation of dose during the first series, as the second series was always identical in each method.

TABLE VIII.—RELATIVE CURE RATE WITH THE OKABAYASHI OPERATION AND POSTOPERATIVE RADIATION

Stage	No. of cases	Survival	Per cent
I	33	30	90.9
II	256	158	61.7
III	44	20	45.5
Total	333	208	62.5

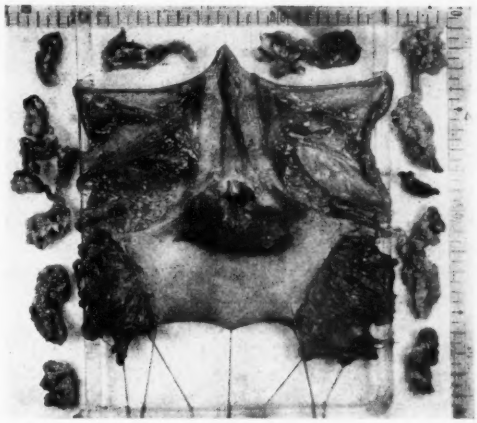

Fig. 2. Specimen of cancerous tumor in advanced stage extirpated by the Okabayashi operation. Cauterization done previous to operation. Extensively dissected pelvic connective tissues and lymph nodes on bilateral sides.

Heyman reported his radiological rate of 34.9 per cent in 1947.

Schmitz reported 28.0 per cent by radiation with 200 kilovolts, but since 1933 with 800 kilovolts roentgen radiation therapy his rate has improved to 43.6 per cent (1933 to 1945). McKelvey, Stenstrom, and Gilliam in 1949 reported a 53.6 per cent cure rate in 297 cases treated radiologically.

My relative cure rate corresponds closely to that of Heyman and Schmitz.

Operative cases.—Table VIII shows the relative cure rate by Okabayashi's operation and Table IX, by abdominal total hysterectomy.

Let us compare Table IX of abdominal hysterectomy with Table VI of radiological cases. In stage I, the rate was 63.6 per cent in the former and 57.5 per cent in the latter. The difference of percentage is statistically not significant. It can be said that total hysterectomy, which I call "simple total"

TABLE IX.—RELATIVE CURE RATE WITH ABDOMINAL HYSTERECTOMY AND POSTOPERATIVE RADIATION

Stage	No. of cases	Survival	Per cent
I	33	21	63.6
II	6	1	16.7
III	1	0	0
Total	40	22	55.0

hysterectomy, cannot be approved as a cancer operation even for an incipient stage. This operation has been abandoned in favor of Okabayashi's operation.

What is the result of the Okabayashi operation? Table VIII demonstrates the rate of the result in stages I, II, and III; we can compare it with Table IX of total hysterectomy and Table VI of radiological cases. For stages I and II operation is definitely better than radiation. The relative 5 year cure rate of 90.9 per cent in cases of stage I suggests that a high percentage of cervical cancer can be cured by extensive radical hysterectomy and pelvic lymphadenectomy followed by post-radiation therapy, if it is treated early. For stage III, the rate seems a little better than that of radiation, but it is not significant statistically. In recent years the primary mortality of Okabayashi's operation has been reduced. In 1950 it was 3 per cent, which is approximately the primary mortality in radiation therapy. Meigs stated recently in his report on 85 cases of radical hysterectomy and dissection of lymph nodes (1939 to 1946) that his relative cure rate was 80.7 per cent for stage I and 60.7 per cent for stage II without postoperative radiation. I conclude that the best method of treatment for cancer of the cervix uteri is first to discover a patient in an early stage of the disease and then to employ the Okabayashi operation, if the patient is in good physical condition, and follow it by radiation therapy.

CONCLUSIONS

1. In the treatment of cancer of the cervix uteri the Okabayashi operation was adopted and applied in 333 cases.

2. The relative 5 year cure rate with this operation was 90.9 per cent for stage I and 61.7 per cent for stage II. These figures are better than the average rates obtained by radiation therapy.

3. The relative 5 year cure rate with simple total hysterectomy was 63.6 per cent for stage I, which was approximately the same as that of radiation, and was statistically not significantly different.

4. In the radiation group, the best relative 5 year cure rate, 42.2 per cent, was obtained by a combination of roentgen deep radiation, radium, and Schaefer's intravaginal cone radiation.

5. An operation, as described by Okabayashi, which is an extensive radical hysterectomy with complete pelvic lymphadenectomy, followed by postoperative radiation, is definitely more effective than radiation treatment alone in early cases.

REFERENCES

1. Coutard, H. Zusammenfassung der Grundlagen der roentgentherapeutischen Technik der tiefgelegenen Krebse. Strahlentherapie, 1930, 37: 50–58.
2. Heyman, J. Improvement of results in treatment of uterine cancer. J. Am. M. Ass., 1947, 135: 412–416.
3. McKelvey, J. L., Stenstrom, K. W., and Gilliam, J. S. Results of experimental therapy of carcinoma of cervix. Am. J. Obst., 1949, 58: 896–907.
4. Meigs, Joe V. Radical hysterectomy with bilateral pelvic lymph node dissection; report of 100 patients operated on 5 or more years ago. Am. J. Obst., 1951, 62: 854.
5. Okabayashi, H. Radical abdominal hysterectomy for cancer of the cervix uteri. Surg. Gyn. Obst., 1921, 33: 335.
6. Idem. Abdominale Systematische Panhysterektomie bei Karzinom des Uterus. Jap. J. Obst., 1928, 11: 136–153; Ber. ges Gyn., 1929, p. 387.
7. Schmitz, H. E. End results of radiation treatment of cancer of the cervix uteri. Am. J. Roentg., 1951, 65: 715.

CONGENITAL DUPLICATIONS OF THE SMALL INTESTINE

Report of 11 Cases

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THE multiplicity of descriptive terms applied to congenital mesenteric cysts of presumed enteric origin has resulted from their wide variance in location, size, and morphologic characteristics, as well as from the lack of a clear embryologic explanation of their occurrence. Most recent authors have elected to classify these anomalies as duplications of the alimentary tract. Although Reginald Fitz, in 1884, was one of the earliest to employ the term duplication, the excellent study of this problem by Ladd and Gross has, perhaps, done more to influence the current acceptance of it.

It is unlikely that these malformations are as rare as they were once thought to be. Indeed, Donovan and Santulli, in 1947, encountered 6 duplications during a period of only 19 months. In a comprehensive review of the literature, LoPresti, Kaufman, and Hawfield found 150 cases of alimentary tract duplication recorded up to 1950. Of this number, 115 (77 per cent) were found in the small intestine. Twenty-seven new cases of small bowel duplication have been added to the literature quite recently by Gross, Holcomb, and Farber (12).

Most of the early cases were recorded as postmortem findings. Fraenkel's necropsy observation, in 1882, of a duplication of the terminal ileum in an 11 day old infant who had died of intestinal obstruction has generally been regarded as the earliest description of a duplication of the small intestine. However, in his review of 1884, Fitz gave priority to the case included in the 1733 essays of Calder.

Although duplications generally cause symptoms during the first decade of life, they may occasionally become symptomatic during later years or pass unnoticed until their accidental discovery on laparotomy or postmortem examination. The most frequently encountered symptoms are those of intestinal obstruction, melena and anemia, and abdominal pain. These symptoms may result from mechanical obstruction of the adjacent intestine or interference with its blood supply by a distended duplication, from peptic ulceration and inflammation, or from the duplication acting as the leading point of an intussusception.

Duplications of the small intestine occur in the mesenteric border of the intestine and may be either spherical or elongated, tubular structures. They are characterized by a smooth muscle coat and a lining of mucous membrane which may resemble that of the adjacent intestine or of some other segment of the alimentary tract. In some cases, more than one type of mucous membrane may be found on careful microscopic examination. The duplication generally has a blood supply in common with the adjacent intestine to which it is intimately adherent. This fact complicates the surgical management of duplications and, for this reason, simple excision is rarely possible. Resection of the duplication and adjacent intestine, followed by primary anastomosis, is currently regarded as the most effective method of treatment. Although Sprengel reported the first successful case of resection in 1900, the mortality from resection as late as 1934 was 79 per cent (11 of 14 cases) (15). However, recent results have been considerably more encouraging.

Owing to the gravity of the problem faced and the limited number of recorded cases, it has been felt desirable to report 11 cases of duplication of the small intestine, 2 of them being of the intramural type. The cases have been divided into two groups, those in which operation was carried out for symptoms resulting from the presence of the duplication

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Fig. 1. Photographs showing the noncommunicating, tubular duplication and adjacent ileum in Case 1, before and after sectioning.

and those in which the duplication was discovered as an incidental operative or postmortem finding.

CASE REPORTS

Symptomatic Duplications Treated Operatively

CASE 1. The patient, a 15 year old white male, was admitted to the hospital, for the fourth time, on October 18, 1943 because of nausea, vomiting, and intermittent crampy abdominal pain of 3 days' duration. He had been under treatment during the previous 5 years for bilateral, saccular bronchiectasis. He had experienced 2 similar episodes during the 2 years prior to admission. On one occasion, a right lower quadrant abdominal mass was felt and intussusception was suspected. His symptoms, however, disappeared following a negative barium enema and no further studies were carried out.

On admission, right lower quadrant tenderness, spasm, and fullness were found. The white blood count was 15,000 with a shift to the left. A tentative diagnosis of acute appendicitis was made and exploration through a McBurney incision was carried out on October 19. Several loops of dilated small intestine and numerous adhesions were encountered. The appendix could not be found and adequate exploration could not be carried out due to the type of incision and the presence of multiple, dense adhesions. It was felt that there was a partial obstruction of the distal ileum. The incision was closed. Parenteral fluid and electrolyte maintenance and Miller-Abbott tube suction were employed until the signs of partial intestinal obstruction had diminished. Oral sulfasuxidine was started on October 28.

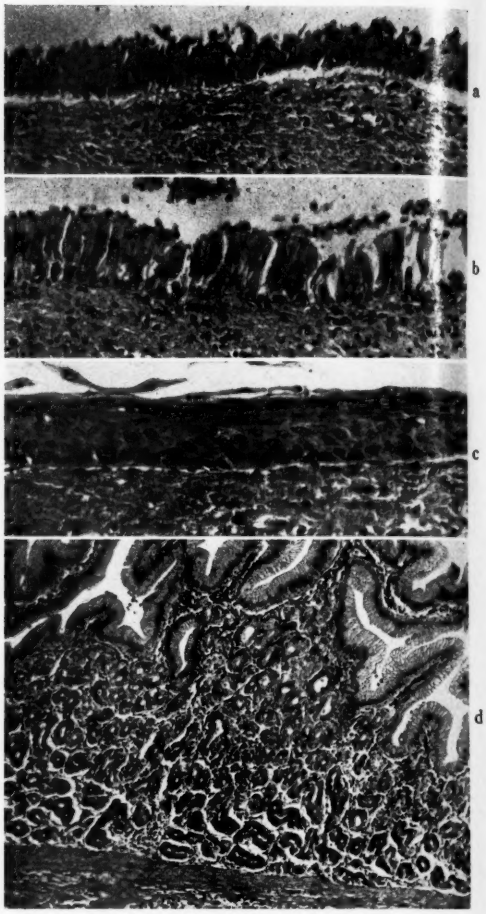

Fig. 2. Photomicrographs of different types of epithelium encountered lining Case 1 duplication: a, transitional epithelium; b, tall columnar epithelium; c, stratified squamous epithelium; d, gastric mucosa.

The patient was re-explored on November 6, through a lower right rectus incision. Numerous adhesions were found and divided. A duplication of the distal ileum was discovered between the leaves of the mesentery approximately 30 centimeters from the ileocecal junction. The duplication was 8 centimeters in diameter and 30 centimeters in length (Fig. 1). It was intimately adherent to the adjacent ileum.

Fig. 3. Photograph of sectioned tubular duplication and adjacent ileum in Case 2 showing the distal communication and the intimate approximation of their walls.

Furthermore, there was a common blood supply to both the ileum and duplication. For this reason, approximately 60 centimeters of ileum were resected with the duplication. The ends of the ileum were closed and a side-to-side anastomosis was carried out. The appendix was also removed.

The postoperative course was complicated only by a small wound abscess which was drained. The patient was asymptomatic when discharged from the hospital on December 18 and he was followed for 2 years without recurrence of abdominal complaints.

On gross examination, no communication was found between the duplication and the ileum. The duplication was distended with a turbid, pink, semifluid material in which there were several blood clots. Three well defined circular folds projected 1 to 2 centimeters into the lumen. In several areas the mucosa had a granular, ulcerated appearance. Microscopically, there was considerable variance in the type of lining of the duplication. Typical gastric mucosa was encountered in several areas. In addition, other areas were lined either by tall columnar cells, by stratified squamous epithelium, or by epithelium resembling that of the transitional type (Fig. 2). Portions of the duplication showed evidence of rather extensive inflammation and ulceration. The walls of the duplication were composed of layers of smooth muscle.

CASE 2. The patient, a 16 month old white female, was admitted to the hospital on December 9, 1944 because of severe anemia associated with intermittent episodes of vomiting and gross melena since 6 weeks of age. Except for obvious pallor, the findings on physical examination were within normal limits. No abdominal masses were palpated. The hemoglobin was 5 grams, the red blood count 2.8 million and the white blood count 11,600 with a normal differential. The bleeding and clotting times, the platelet count and the red cell fragility were normal. The urine was also normal. No abnormalities were encountered on either barium enema or upper gastrointestinal roentgenographic studies. The hemoglobin and red blood count were returned to normal following several small whole blood transfusions.

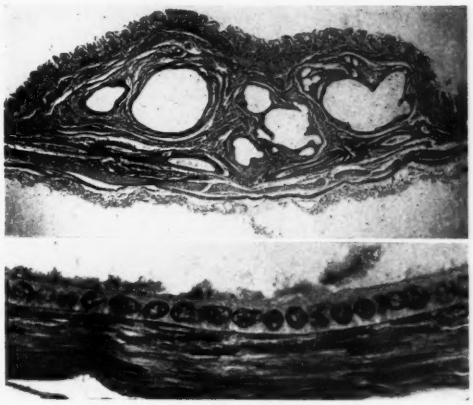

Fig. 4.

Fig. 5.

Fig. 4. Photomicrographs showing the area of multiple intramural enteric cysts in Case 8 with a more highly magnified view of the epithelial lining and smooth muscle coat of one of the cysts.

Fig. 5. Photomicrograph of the 1 large and several small intramural enteric cysts in Case 9 with a portion of the lining of the large cyst under high power.

On January 4, the peritoneal cavity was entered through an oblique incision in the lower abdomen. A duplication of the ileum measuring 40 centimeters in length and 3 centimeters in diameter was found approximately 75 centimeters from the ileocecal junction. The duplication was located between the leaves of the mesentery and was partially adherent to the adjacent ileum. It was felt that the patient was not properly prepared for a bowel resection and the ab-

domen was closed. Oral sulfasuxidine was started 3 days postoperatively and 9 days later the patient was re-explored. Approximately 45 centimeters of ileum were resected with the duplication. The ends of the ileum were closed and a side-to-side anastomosis was carried out. The postoperative course was uncomplicated and the patient was discharged from the hospital. She has been asymptomatic since discharge.

The distal end of the duplication communicated with the ileum and the proximal end was closed (Fig. 3). There was a common blood supply to both the ileum and duplication. Microscopically, the wall of the duplication was composed of an outer longitudinal and an inner circular smooth muscle coat. It was lined with gastric mucosa. Several scattered areas of ulceration were also identified.

CASE 3. The patient, a 5 month old white male, was admitted to the hospital on September 15, 1945 because of severe anemia associated with melena of 3 weeks' duration. Marked pallor was noted on examination. There was considerable rigidity of the abdominal wall and no masses could be palpated. The hemoglobin was 7 grams, the red blood count 2.2 million and the white blood count 14,000. The platelet count was within normal limits. The barium enema was reported as normal, as was the upper gastrointestinal study. There was, however, a slight residue of barium in the distal ileum at the end of 6 hours. Several whole blood transfusions were given and oral sulfasuxidine was started on September 22.

The infant was taken to the operating room on September 27 and the peritoneal cavity was entered through a right midrectus incision. Several loops of small intestine were adherent to the anterior abdominal wall. The most intimately adherent loop was inadvertently opened and the presence of a congenital duplication of the ileum was confirmed. The duplication measured approximately 60 centimeters in length. The adjoining ileum was resected with the duplication and an end-to-end anastomosis was carried out. A small amount of mucosa was left adherent to the abdominal wall and this was covered with omentum.

The operation was well tolerated. Gastric suction and parenteral maintenance were employed postoperatively and both penicillin and sulfadiazine were given. Except for a temperature elevation to 103 degrees on the third and fourth postoperative days, the hospital course was essentially uncomplicated. The patient was discharged on November 9 and was asymptomatic during 3 years of outpatient clinic observation.

On gross examination both the proximal and distal ends of the duplication were found to communicate with the ileum. Microscopically, it had a smooth muscle coat of 2 layers and was lined with gastric mucosa.

CASE 4. The patient, a 6 month old white male, was admitted to the hospital on December 25, 1946 because of vomiting of 4 days' duration associated with obstipation and some mild abdominal distention. He appeared pale, dehydrated, and listless. His abdomen was soft on examination and a mass was palpated in the left lower quadrant. Peristalsis was hyperactive and high pitched. A mass was also palpable on rectal examination. There was, however, no evidence of melena. The hemoglobin was 11 grams and the white blood count 8,500 with a normal differential. Survey abdominal roentgenograms showed findings consistent with small intestinal obstruction. Barium enema examination showed a definite cuff, indicating an intussusception, in the distal descending colon. Efforts at barium enema reduction were unsuccessful (21).

The abdomen was opened on the day of admission. An ileocolic intussusception was found with the intussusceptum at the splenic flexure. It was easily reduced by taxis. A mass, measuring 3 centimeters in diameter, was found to be adherent to the mesenteric border of the terminal ileum. It was apparent that this mass had been the leading point of the intussusception. The mass was resected with the terminal ileum and the cecum. The ends of the ileum and colon were closed and a side-to-side anastomosis was carried out between the distal ileum and the proximal ascending colon.

Gastric suction and parenteral alimentation were carried out postoperatively. Penicillin was given. The postoperative course was uncomplicated and the patient was discharged from the hospital 13 days following operation.

On opening the gross specimen, there was no apparent communication between the duplication and the ileum. Histologically, the duplication was lined with colonic mucosa. The thick smooth muscle of wall of the duplication was arranged in a disorderly manner with no clear differentiation into circular and longitudinal layers. In the subserosa of the ileum, several small gland spaces bearing resemblance to the mucosa of the colon were identified.

CASE 5. The patient, an 11 year old white female, was admitted to the hospital on February 17, 1949 because of continuous abdominal pain and melena of 2 weeks' duration associated with nausea and vomiting. She had suffered from intermittent attacks of poorly localized abdominal pain and melena since the age of 2 years. Tenderness in the right lower quadrant was elicited on deep palpation. No abdominal masses were felt. A tarry stool, which was positive for blood, was discovered on rectal examination. The patient's hemoglobin on admission was 8.5 grams, the red blood count 2.9 million and the white blood count 6,100 with a normal differential. The bleeding and clotting times, the platelet count, and the prothrombin time were within normal limits. The urine was normal. There were no abnormal findings on roentgenographic barium studies of the upper gastrointestinal tract and the colon. Sigmoidoscopy was also negative.

Exploration through a low midline incision was carried out on February 28. A duplication of the ileum, measuring 35 centimeters in length, was found approximately 40 centimeters from the ileocecal

junction. The omentum was adherent to the distal end of the duplication, at the site of an old, walled-off perforation. There was a common blood supply to both the ileum and duplication. The duplication and the adjacent ileum were resected. The ends of the remaining ileum were closed and a side-to-side anastomosis was performed. The patient tolerated the procedure well and her postoperative course was completely uneventful. She was discharged from the hospital 9 days following operation and has remained asymptomatic.

On gross examination, there was a communication between the distal end of the duplication and the ileum and an area of ulceration was found at the site of the communication. Microscopically, the duplication was lined with gastric mucosa. There was some mild irregularity of the smooth muscle wall of the duplication, possibly due to the presence in it of several areas of isolated mucous glands.

CASE 6. The patient, a 67 year old white male, was admitted to the hospital on August 21, 1950 for repair of a direct right inguinal hernia. He had had no previous gastrointestinal symptoms. Only a right inguinal hernia and bilateral lower extremity varicose veins were found on examination. There were no palpable abdominal masses. The admission laboratory studies were within normal limits. A right inguinal herniorraphy was performed under spinal pontocaine anesthesia on August 23. The patient's abdomen became markedly distended the day following operation and there was radiologic evidence of a large accumulation of both large and small bowel gas. The distention was relieved by gastrointestinal suction and repeated enemas. Barium enema studies revealed the presence of a constant filling defect in the cecum. It was suspected that carcinoma of the cecum was present, and oral sulfasuxidine was started on September 6.

On September 12, the patient was taken to the operating room and the peritoneal cavity was entered through a right midrectus incision. A duplication, measuring approximately 8 centimeters in diameter, was found to be adherent to the terminal ileum. The distal end of the duplication was only 3 centimeters from the ileocecal junction. There was a common blood supply to both the ileum and duplication. Approximately two thirds of the cecum and 15 centimeters of the terminal ileum were resected with the duplication. The ends of the ileum and cecum were closed and a side-to-side anastomosis was carried out. The postoperative course was uneventful and the patient was discharged from the hospital 8 days following the operation. He has remained asymptomatic.

On gross examination, the duplication was found to be filled with yellowish mucous material. It was adherent to the terminal ileum which was flattened out over it. There was no communication between the duplication and the ileum. Histologically, the wall of the duplication was formed by 2 layers of smooth muscle and it was lined both by colonic mucosa and by flattened epithelial cells.

Asymptomatic Duplications as Incidental Findings at Operation or Necropsy

CASE 7. The patient, a 36 hour old premature white female weighing 4 pounds and 10 ounces, was admitted to the hospital on April 15, 1947 because of jaundice and persistent vomiting since birth. There was no abdominal distention and no masses were palpable. The hemoglobin was 19 grams, the red blood count 6.2 million and the white blood count 9,000. Roentgenograms suggested the presence of complete duodenal obstruction. The patient was explored on April 17 and was found to have a midgut volvulus, due to a congenitally short mesentery, with 2 rather extensive areas of gangrene in the proximal jejunum and distal ileum. The gangrenous jejunum ruptured during derotation. A small mass, 1.5 centimeters in diameter, was encountered, as an incidental finding, in the mesentery of the jejunum. The mass was included with one of the 2 gangrenous segments of small intestine which were resected. The continuity of the intestinal tract was re-established by 2 anastomoses. The patient died 10 days following operation. The wall of the duplication was composed of smooth muscle layers and it was lined with jejunal mucosa. There was no apparent communication between the duplication and the adjacent jejunum.

CASE 8. The patient was a 3 month old white male who was admitted to the hospital on September 17, 1938 with bronchopneumonia and bilateral otitis media. Shortly after admission, his temperature rose to 106 degrees and he died on September 20. In the terminal ileum there was an area of approximately 1 centimeter in diameter in which the inner circular muscle layer contained several cysts lined with cuboidal epithelium (Fig. 4). Each cyst was completely surrounded by its own layer of smooth muscle. Sections of the ileum, other than those through the cystic area, revealed the presence of many small collections of apparently isolated epithelial cells in the connective tissue between the muscularis mucosa and the circular smooth muscle layer. Some of these cells seemed to be arranged in the form of rudimentary glands.

CASE 9. The patient was a 1 month old white male who was admitted to the hospital on November 29, 1941 because of vomiting and convulsions associated with myelomeningocele and hydrocephalus. He died 6 days later and was found, in addition, to have a purulent meningitis and bronchopneumonia. Microscopic examination of one section of ileum revealed one large cyst and a number of small ones lined with both cuboidal and columnar epithelium (Fig. 5). Each cyst was, at least partially, surrounded by its own coat of smooth muscle. The cysts were located between the muscularis mucosa and the circular muscle layer. The smooth muscle bundles in this area appeared rather disorganized and there was considerable interlacing of bundles.

CASE 10. The patient was a 59 year old white male who was admitted to the hospital on February 18, 1947 because of fever, cyanosis, and dyspnea. He died 4 hours after admission and was found on ne-

cropsy to have extensive pulmonary tuberculosis. Immediately distal to the pylorus there was a swelling which appeared, at first, to be due to a dilatation of the first portion of the duodenum. On closer examination, the duodenum was of normal size but was intimately adherent to a round, cystic mass measuring 8 centimeters in diameter. The duplication did not communicate with the duodenum. Its wall was composed of fibrous tissue and irregular bundles of smooth muscle. The lining of the duplication could not be found in the available sections.

CASE 11. The patient was a 42 year old white female who was admitted to the hospital on September 4, 1948 because of hemorrhagic shock due to profuse vaginal bleeding. An advanced carcinoma of the cervix was found to be the cause of her blood loss. During examination, the patient complained of severe chest pain and died 2 hours after admission. Squamous cell carcinoma of the cervix and ischemic degeneration and focal necrosis of the myocardium were found on necropsy. A small nodular mass was discovered in the mesenteric border of the ileum approximately 10 centimeters from the ileocecal junction. The duplication was 1.5 centimeters in diameter. It had a smooth muscle coat and was lined by cuboidal epithelium. There were numerous bundles of smooth muscle in this area which were interlacing and apparently lacking in organization.

DISCUSSION

The embryologic explanation of the occurrence of alimentary tract duplications is rendered especially difficult by their unusually wide variation in structure and location. Three principal theories, none of them completely adequate, have been advanced. The earliest theory to achieve any degree of acceptance regarded duplications to be of omphalomesenteric duct origin. This theory, however, fails to explain the occurrence of hindgut and foregut duplications. Furthermore, omphalomesenteric duct anomalies occur on the antimesenteric border of the intestine, whereas duplications are found on the mesenteric border. Two cases have been reported, by Edwards and Grove and Porch, in which both a duplication and a Meckel's diverticulum were present.

Keibel, in 1905, and Lewis and Thyng, in 1908, independently described the presence of small subendothelial diverticula as a constant feature of embryonic development toward the end of the second month. These diverticula were most frequently encountered in the ileum and normally disappeared. It was suggested that the persistence and pinching off of one of these diverticula might produce a duplication. However, the diverticula are generally found on the antimesenteric border of the intestine.

Although Bremer believed that the diverticula theory might account for the formation of spherical duplications, he found this theory unsatisfactory for tubular duplications. He, accordingly, concluded that spherical and tubular duplications were separate entities embryologically, each being formed in a different manner. He suggested that the observations of Johnson concerning the formation of intercellular vacuoles during the so-called "solid" stage of alimentary tract development in the sixth embryonic week, might more adequately explain the production of tubular duplications. These vacuoles could become fused into chains and, through retention of their form, result in the formation of a tubular duplication.

Both the diverticula and the confluent vacuolization theories are concerned principally with local phenomena and, hence, do not account satisfactorily for the frequent presence of gastric and other mucosal linings dissimilar to that of the adjacent intestine nor do they account for the large intrathoracic diverticula which originate from the small intestine. It is also possible that the misplaced gastric tissue, so frequently encountered as the lining of tubular duplications, might represent aberrant stomach, a "duplication" of the stomach, just as misplaced pancreatic tissue along the alimentary tract is looked upon as aberrant pancreas regardless of its location. This method of reasoning might also be applied to other types of epithelial lining which differ from that of the adjacent intestine. Although several interesting and, in many respects, worthy theories have been advanced, the genesis of these fascinating congenital deviations from the normal intestinal morphology is by no means settled.

Congenital cysts of the mesentery must be differentiated from those of traumatic, neoplastic and infectious origin. The congenital group includes dermoid cysts, the large flabby serous or chylous cysts of presumably lymphatic origin, and enterogenous cysts. Because of their unusually wide variance both structurally and symptomatically, a further subdivision of enteric cysts is necessary:

TABLE I.—SUMMARY OF FINDINGS IN CASES OF ASYMPTOMATIC DUPLICATION

Case Sex	Age	Location	Shape	Size, cm.	Communication with adjacent intestine	Lining of duplication
7 Female	36 hours	Jejunum	Spherical	1.5	o	Jejunal mucosa
8 Male	3 months	Terminal ileum (intramural)	Spherical (multiple)	1.0	o	Cuboidal epithelium
9 Male	1 month	Ileum (intramural)	Spherical (multiple)	0.8	o	Cuboidal epithelium Columnar epithelium
10 Male	59 years	Duodenum	Spherical	8	o	Not identified
11 Female	42 years	Terminal ileum	Spherical	1.5	o	Cuboidal epithelium

(1) intramural cysts; (2) spherical duplications; (3) tubular duplications; (4) thoracoabdominal diverticula originating from the small intestine; (5) free mesenteric cysts with smooth muscle walls. We have observed significant clinical and pathological differences between spherical and tubular duplications and these observations would appear to support Bremer's concept that these two forms of duplication differ in their embryologic development.

Recently, 4 cases of large intrathoracic diverticula, or duplications, originating from the small intestine have been reported, 3 by Gross, Neuhauser, and Longino (13) and 1 by Fisher. One of these diverticula originated from the duodenum, 2 from the jejunum, and 1 from the ileum. All 4 entered the thoracic cavity through the right diaphragm and they all communicated with the small intestine. Three of the 4 were lined with gastric mucosa and all 4 were successfully removed by staged abdominal and thoracic operations. These diverticula, from their tubular form, their distal communication with the small intestine, and the frequency of their lining with gastric mucosa, would appear to be rather closely related to the tubular type of duplication which runs the bulk of its course within the leaves of the mesentery.

It should be emphasized, at this point, that separate intestinal and mediastinal duplications may also occur in the same case. Roth in 1881, reported one of the earliest instances of the simultaneous presence of separate duplications of the small intestine and esophagus. Others have been reported since that time. Indeed, LoPresti and his associates have recently estimated that approximately one half of the reported mediastinal duplications were associated with intra-abdominal duplications. The experience at this institution with esophageal duplication has been reported elsewhere by one of the authors (1).

The majority of the asymptomatic enteric cysts in our series were small and none of them communicated with the intestine (Table I). Two of these cysts were of the intramural type and they were lined by a simple cuboidal or columnar epithelium which did not tend to simulate the mucosal pattern of any segment of the gastrointestinal tract. Even when the cysts were multiple, each cyst appeared to have its own circular smooth muscle coat. Varying degrees of irregularity and interlacing of smooth muscle bundles were frequently found. In Case 8, examination of sections of ileum, other than the one through the cystic area, revealed the presence of numerous small clusters of apparently isolated epithelial cells in the connective tissue between the muscularis mucosa and the circular muscle layer. Similar findings were encountered in Cases 4 and 5. It is unlikely that these small cysts would cause difficulty except, possibly, as the leading point for an intussusception.

One of the authors (22) has recently reported, from this hospital, 3 cases of large mesenteric cysts, the walls of which contained irregular and interlacing bundles of smooth muscle. The cells lining the cysts were considerably flattened, presumably due to the great size and distention of the cysts. None of the cysts was adherent to the intestine and the suggestion was made that some of these free mesenteric cysts might be of enteric deriva-

TABLE II.—SUMMARY OF FINDINGS IN CASES OF SYMPTOMATIC DUPLICATION

Case Sex	Age	Symptoms	Location	Shape	Size* cm.	Communications with adjacent intestine	Lining of duplication
1 Male	15 years	Obstruction, inflammation	Ileum	Tubular	30	0	Gastric mucosa, columnar cells, stratified squamous, transitional epithelium
2 Female	16 months	Melena, anemia	Ileum	Tubular	40	1 distal	Gastric mucosa
3 Male	5 months	Melena, anemia, inflammation	Ileum	Tubular	60	1 distal 1 proximal	Gastric mucosa
4 Male	6 months	Intussusception	Terminal ileum	Spherical	3	0	Colonic mucosa
5 Female	11 years	Melena, anemia, inflammation	Ileum	Tubular	35	1 distal	Gastric mucosa
6 Male	67 years	Obstruction	Terminal ileum	Spherical	8	0	Colonic mucosa, flattened epithelial cells

*Measurement of length given for the tubular forms and that of diameter for the spherical.

tion, while others were of the more generally accepted lymphatic origin.

Although the symptoms associated with a duplication of the small intestine may occasionally arouse an active suspicion of its presence, the diagnosis generally must be based on its operative identification. There is no clear evidence of any significant sex or race incidence of duplications. Symptoms generally arise during infancy or childhood. Roentgenologic studies are rarely of diagnostic value and abdominal palpation is only occasionally rewarding. Excluding the case in which the palpable mass was that of an intussusception, an abdominal mass was palpated in only 1 of our other 5 symptomatic cases. Five of the duplications of Donovan and Santulli involved the small bowel and in none of these cases was a mass palpated. Although Ladd and Gross suggested, from their experience, that a mass could usually be felt, they gave no figures to indicate the frequency of palpability in their series.

There has also been some difference of published opinion relative to the incidence of communication between the duplication and the adjacent intestine. Ladd and Gross have stated that "a great majority of the specimens do not possess a communication with the alimentary tube." Donovan and Santulli, on the other hand, found a communication in 4 of their 5 cases and observed, from their cases and from a review of the literature, that the elongated type of duplication generally communicated distally with its proximal portion ending blindly in the mesentery. A communication was encountered in 3 of our group of 6 symptomatic cases (Table II). None of the spherical duplications communicated with the intestine, whereas 3 of the 4 tubular duplications did. From a review of these and other reported cases, it becomes quite apparent that a majority of the tubular duplications communicate with the adjacent intestine while the spherical ones seldom do. This finding accounts for the divergence of opinion concerning the frequency of communication. The majority of the duplications seen by Ladd and Gross were of the spherical type, whereas the bulk of those studied by Donovan and Santulli and by us were tubular.

An additional finding of considerable interest concerns the symptomatic and microscopic differences between spherical and tubular duplications. All 4 of our tubular duplications were lined with gastric mucosa. Neither of the 2 symptomatic spherical duplications contained gastric mucosa nor was it encountered in any of the 5 asymptomatic enteric cysts, all of which were spherical. A review of the reported cases of tubular duplication reveals that the great majority of them contained gastric mucosa. It was found in all of the 3 tubular duplications of Donovan and Santulli and in the 2 of Ripstein. In both of the 2 clear cut cases of Ladd and Gross the tubular duplication was lined by gastric mucosa. Of the 6 new cases of tubular duplication added by Gross, Holcomb, and Farber (12), 4 were lined with gastric mucosa. Gastric mucosa was also found in the tubular duplications reported by Edwards, Poncher and Milles, and Black and

Benjamin. Furthermore, there appears to be a tendency for some of the tubular duplications to be lined by more than 1 type of epithelium, as found in our Case 1 and in other reported cases (6, 25). It should, perhaps, be noted again that gastric mucosa was found in 3 of the 4 reported long intrathoracic diverticula from the small intestine since these malformations, in some respects, resemble tubular duplications.

The high incidence of gastric mucosa in tubular duplications is associated with an almost equally high incidence clinically of melena and severe anemia. These symptoms were encountered in 3 of our cases and, in all 3, they were found to be due to peptic ulceration from a communicating tubular duplication lined with gastric mucosa. Symptoms in the case of closed tubular duplication were those of inflammation within the diverticulum and obstruction of the adjacent intestine by distention of the diverticulum. Melena was not a symptom in this case nor was it a symptom in our other case of simple obstruction by a spherical cyst. It would appear, from these and from other reported cases, that melena and anemia generally result from the peptic ulceration associated with a communicating, gastric mucosa lined duplication, usually of the tubular type, rather than from ischemic sloughing of the mucosa of the adjacent intestine due to interference with its blood supply by the duplication as suggested by Ladd and Gross. In 1 of our cases, an old perforated ulcer of the diverticulum, which had been closed by the omentum, was found. Although a similar finding was reported by Black and Benjamin, the hazards of this complication seem to be considerably less than those of the bleeding from peptic ulceration.

Spherical duplications are rather frequently found in the terminal few centimeters of the ileum near the ileocecal junction and it is in this location that they are most likely to become symptomatic. The larger ones generally cause symptoms of intestinal obstruction while the smaller ones tend more often to act as the leading point for an intussusception. Intussusception was described in 6 of the 34 symptomatic cases of duplication reviewed in 1934 by Hughes-Jones. Spherical small bowel duplications of the ileocecal region do not, as a rule, communicate and are generally lined with ileal or colonic mucosa, or both. Occasionally, simple columnar or cuboidal epithelium may be found, rarely gastric. It seems, however, that there is a somewhat higher incidence of both communication and gastric lining in the spherical duplications found more proximally in the ileum and higher in the small intestine. Melena and anemia occur more often in these cases.

TABLE III.—REPORTED RESULTS WITH RESECTION AND PRIMARY ANASTOMOSIS

Author	Date	No. of cases	No. of deaths	Mortality, per cent
Ladd and Gross	1941	6	1	17
Donovan and Santulli	1947	5	0	0
Ripstein	1949	4	2	50
Fisher	1950	2	0	0
Gross, Holcomb, and Farber	1952	13	2	15
Moore and Battersby	1952	6	0	0

Due to the intimate association of the duplication with the adjacent intestine and its blood supply, simple excision is rarely possible. Although by-passing operations and such measures as evacuation of the duplication and marsupialization of it have been suggested, the most satisfactory treatment for small bowel duplications has been shown to be resection of the duplication and its adjacent intestine. The early mortality with resection was quite high and Waugh, discussing a case treated by a Mikulicz type of resection in 1939 (5), advised against primary anastomosis.

All 6 of our symptomatic cases were managed by resection of the duplication and adjacent intestine with primary anastomosis and all 6 recovered. The resection was carried out in 1 case following the successful reduction of an ileocolic intussusception by taxis. Lateral anastomoses were used in 5 cases and an end-to-end in 1. Preresection preparation of the intestines with oral sulfasuxidine was employed in 4 cases and postoperative antibiotics were used in all 6. Gastric suction and parenteral administration of fluids, electrolytes, and whole blood were carried out as indicated. The more recently reported results of other

authors with resection and primary anastomosis have also shown a rather marked reduction in mortality (Table III).

As one might expect, the tubular duplications have often been more difficult to manage surgically than the spherical. The preoperative condition of these patients is generally poorer due to the degree of blood loss and inflammation and a more extensive bowel resection is necessary to remove the tubular duplication. Both patients of Ladd and Gross with tubular duplications died following resection and 2 of the 6 of Gross, Holcomb, and Farber died. One of the 2 patients of Ripstein with tubular duplication also died postoperatively. However, our 4 patients with tubular duplications and the 3 of Donovan and Santulli all recovered.

One additional operative approach deserves mention. Gardner and Hart, in 1935, reported the successful treatment of a duplication of the duodenum by creating a "window" between the duplication and the duodenum and, in this way, effectively establishing internal drainage. This operation was ideal for the case in which it was used because of the technical hazards of an extensive resection in the duodenal area. Gross, Holcomb, and Farber recently reported its use in 2 cases of duodenal duplication. However, its applicability to duplications in other regions is rather limited. Its use would seem to be limited to those noncommunicating, symptomatic (obstructing) duplications which are not lined with gastric mucosa and which are situated in an area where a major resection for a nonmalignant lesion would be considered unwise. This combination of circumstances is rarely encountered in small intestinal duplications and, for practical purposes, resection of the duplication and intestine and primary anastomosis can be considered as the treatment of choice.

SUMMARY

1. The literature concerning congenital duplications of the small intestine is reviewed and it is estimated that approximately 150 cases have been reported up to the present.

2. Eleven new cases of duplication of the small intestine are reported, 2 of them being the intramural type. The cases are divided into 2 groups; those cases, 6 in number, treated operatively because of symptoms associated with the duplication and those in which the duplication was asymptomatic and was encountered as an incidental operative or necropsy finding.

3. Of the 6 symptomatic cases, 3 were admitted because of melena and severe anemia, 2 because of intestinal obstruction, and 1 because of intussusception. Inflammation was also a significant feature in 3 of the cases. Four of the duplications were tubular and 2 were spherical. All 4 tubular duplications were lined with gastric mucosa and 3 of them communicated with the adjacent intestine. Neither of the spherical duplications contained gastric mucosa nor communicated with the intestine.

4. All, but 1, of the asymptomatic duplications were quite small. They were all spherical, and the 2 intramural enteric cysts were multiple. None of these duplications contained gastric mucosa and none of them communicated with the intestine.

5. All 6 symptomatic cases were treated operatively, by resection of the duplication and the adjacent intestine followed by primary anastomosis, without mortality. Oral sulfasuxidine was given preoperatively in 4 of the cases and all 6 received antibiotics postoperatively. Gastric suction and parenteral maintenance with fluid, electrolytes, and whole blood were employed as indicated.

6. The theories of the embryogenesis of alimentary tract duplications are discussed and the dual origin theory of Bremer is regarded as the most satisfactory to date. The spherical and the tubular duplications, in his opinion, differ in the manner of their embryonic formation.

7. A classification of congenital cysts of the mesentery is presented and the enteric group of cysts is subdivided into intramural cysts, spherical duplications, tubular duplications, thoracoabdominal diverticula originating from the small intestine, and free mesenteric cysts with smooth muscle walls.

8. Significant clinical and morphologic differences between the spherical and tubular types of duplication are cited. Although there

are exceptions, it appears that tubular duplications most frequently are found in the ileum, are lined with gastric mucosa, communicate with the adjacent intestine, and produce symptoms of abdominal pain, melena, and severe anemia. Spherical duplications, on the other hand, are often found in the terminal ileum, seldom contain gastric mucosa, and seldom communicate with the intestine. The larger spherical duplications often cause intestinal obstruction while the smaller ones may act as the leading point for an intussusception. There seems to be a greater tendency for spherical duplications to contain gastric mucosa and to communicate with the adjacent intestine when they are located more proximally in the ileum than when they are found in the terminal few centimeters.

9. Resection of the duplication and the adjacent intestine followed by primary anastomosis is recommended as the treatment of choice for the vast majority of congenital duplications of the small intestine. It is suggested that preoperative preparation of the intestinal tract by an antibiotic, such as sulfasuxidine or aureomycin, should be carried out in suspected cases of small bowel duplication.

REFERENCES

1. BATTERSBY, J. S. Duplication of the esophagus. Q. Bull. Indiana Univ. M. Center, 1950, 12: 9.
2. BLACK, R. A., and BENJAMIN, E. L. Enterogenous abnormalities. Am. J. Dis. Child., 1936, 51: 1126.
3. BREMER, J. L. Diverticula and duplications of the intestinal tract. Arch. Path. Chic., 1944, 38: 132.
4. CALDER, J. Medical Essays and Observations. Vol. 1, p. 205. Edinburgh: 1733.
5. DOCKERTY, M. B., KENNEDY, R. L. J., and WAUGH, J. M. Enterogenous cysts. Proc. Mayo Clin., 1939, 14: 664.
6. DONOVAN, E. J., and SANTULLI, T. V. Duplications of the alimentary tract. Ann. Surg., 1947, 126: 289.
7. EDWARDS, H. Congenital diverticula of the intestine. Brit. J. Surg., 1929, 17: 7.
8. FISHER, H. C. Duplications of the intestinal tract in infants. Arch. Surg., 1950, 61: 957.
9. FITZ, R. H. Persistent omphalomesenteric remains; their importance in the causation of intestinal duplication, cyst-formation, and obstruction. Am. J. M. Sc., 1884, 88: 30.
10. FRAENKEL, E. Ueber Cysten im Darmkanal. Virchow's Arch., 1882, 87: 275.
11. GARDNER, C. E., JR., and HART, D. Enterogenous cysts of the duodenum. J. Am. M. Ass., 1935, 104: 1809.
12. GROSS, R. E., HOLCOMB, G. W., and FARBER, S. Duplications of the alimentary tract. Pediatrics, 1952, 9: 449.
13. GROSS, R. E., NEUHAUSER, E. B. D., and LONGINO, L. A. Thoracic diverticula which originate from the intestine. Ann. Surg., 1950, 131: 363.
14. GROVE, E. W., and PORCH, L. D. Duplication of the terminal ileum; report of a case associated with two congenital diverticula. South. M. J., 1943, 36: 735.
15. HUGHES-JONES, W. E. A. Enterogenous cysts. Brit. J. Surg., 1934, 22: 134.
16. JOHNSON, F. P. The development of the mucous membrane of the oesophagus, stomach and small intestine in the human embryo. Am. J. Anat., 1910, 10: 521.
17. KEIBEL, F. Zur Embryologie des Menchen, der Affen, und der Halbaffen. Anat. Anz. (Supp.), 1905, 27: 39.
18. LADD, W. E., and GROSS, R. E. Abdominal Surgery of Infancy and Childhood. Philadelphia: W. B. Saunders Co., 1941.
19. LEWIS, F. T., and THYNG, F. W. The regular occurrence of intestinal diverticula in embryos of the pig, rabbit, and man. Am. J. Anat., 1908, 7: 505.
20. LOPRESTI, J. M., KAUFMAN, P., and HAWFIELD, H. H. Duplication of the alimentary tract. Clin. Proc. Child. Hosp., Wash., 1950, 6: 357.
21. MOORE, T. C. The management of intussusception in infants and children. Ann. Surg., 1952, 135: 184.
22. Idem. Congenital cysts of the mesentery; report of three cases. Q. Bull. Indiana Univ. M. Center, 1952, 14: 36.
23. PONCHER, H. G., and MILLES, G. Cysts and diverticula of intestinal origin. Am. J. Dis. Child., 1933, 45: 1064.
24. RIPSTEIN, C. B. Duplications of the small intestine. Am. J. Surg., 1949, 78: 847.
25. ROTH, M. Ueber Missbildungen im Bereich des Ductus omphalomesentericus. Virchow's Arch., 1881, 86: 371.
26. SPRENGEL. Ein angeborene Cyste der Darmwand als Ursache der Invagination. Arch. klin. Chir., 1900, 61: 1032.
27. WAUGH, J. M. Discussion of paper by Dockerty, M. B., Kennedy, R. L. J., and Waugh, J. M. (5).

INTESTINAL OBSTRUCTION IN THE NEWBORN ASSOCIATED WITH FAULTY DEVELOPMENT OF THE MIDGUT AND ITS MESENTERY

A Description of Three Cases

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THIS article presents an account of 3 cases of acute intestinal obstruction in neonates. They are grouped together since they all have one common feature, namely inadequate fixation of the midgut and its mesentery to the posterior abdominal wall. All 3 infants were found to have some kind of volvulus of the intestine and the third was complicated by atresia or stenosis of the intestine.

CASE REPORTS

CASE 1. The patient, P.I., female, was first seen at Alder Hey Children's Hospital on February 3, 1951, when she was 1 week old. She was born at home on January 27, 1951 after a gestation lasting 38 weeks. Delivery was normal and her birth weight was 8 pounds. Meconium was passed normally after birth. She was fed at the breast from birth, supplemented with additional feeds of glucose. Both parents were healthy and a brother, aged 3½ years, was also healthy.

The mother noticed that the baby suffered a great deal from flatulence and frequent posseting. Vomiting first occurred on January 31, 1951, 5 to 10 minutes after being fed. The vomiting was described as "forceful." The color of the vomit was yellow. It occurred twice on January 31, 1951 and on each occasion was described as projectile. The bowels were opened two or three times each day from birth except on January 30, 1951. On this day she had frequent thin yellow stools. This was attributed to the mother having taken an excessive amount of purgative in the form of senna and double strength Seidlitz powder. She came into the hospital for observation on February 3, 1951. Her weight on admission was 7 pounds. Examination revealed no abnormal physical signs. She seemed quite healthy and there were no signs of dehydration. There was no abdominal distention. There was no inflammation of the umbilicus. The liver and spleen were not enlarged. She settled down well in hospital. She was put on a regimen of expressed breast milk, 2 ounces, 3 hourly, 7 feeds in 24 hours on February 3, 1951 and this was increased to 2½ ounces on February 4, 1951 and February 5, 1951. No vomiting occurred and she was taken home by her mother on February 6, 1951. The baby's weight on discharge on February 6, 1951 was 6 pounds 14 ounces.

At home she was given an average of 6 feeds of Ostermilk No. 1. (3 measures to 3 ounces of water) per day, with occasional early morning or night breast feed. She posseted occasionally but there was no vomiting during the next 4 days. She was constipated and no stool was passed during the first 3 days after discharge from hospital. Thereafter 1 constipated stool was passed daily. On February 12, 1951, vomiting took place 3 times: at 10:30 a.m. and twice after the 4:30 p.m. feed. Vomit was said to be projectile. It occurred during the first half hour after a feed and the color of the vomited material was yellow. The mother observed that she took the first 2 ounces of feed well, but then lost interest and appeared apathetic and indifferent.

On February 13, 1951 she was brought back to hospital by the parents. She seemed to be fretful and vomited a little while being examined. This vomit was not projectile. She was readmitted for further investigations. There were no abnormal physical findings on admission. The respiratory, cardiovascular, and central nervous systems were normal. The ears, nose, and throat were also normal.

There were no abnormal findings in the abdomen. Distention was absent. No visible peristalsis was observed and no mass or tumor could be palpated. Following a rectal examination a small constipated stool slightly stained with fresh blood was passed. Her weight on February 14, 1951 was 7 pounds 4½ ounces. She vomited after feeding with half cream National Dried Milk at 6:00 a.m. and again after a glucose feed at 11:00 a.m. Two small constipated yellow stools were passed during the morning. Glucose water given by mouth at 1:00 p.m. was kept down. Glucose water given at 3:00 p.m. was vomited. Abdominal examination revealed visible gastric peristalsis and a suspicion of a ladder pattern on the right side of the abdomen. No pyloric tumor could be felt. There was no abdominal distention.

On February 14, 1951 roentgenograms were taken of the abdomen in supine and erect positions. Both films showed the stomach distended with gas. In the

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erect film a level extending across the upper abdomen suggested an obstructed loop of intestine (Figs. 1, 2).

Continuous gastric aspirations by means of a soft rubber catheter passed nasally and intravenous therapy were instituted on February 14, 1951 on account of dehydration and vomiting. A total of 125 cubic centimeters of bile-stained fluid was aspirated in the first 24 hours. Fluid requirements for 2 hours were estimated at 140 cubic centimeters of half strength plasma, 140 cubic centimeters of Hartmann's solution in 5 per cent dextrose and 245 cubic centimeters of fifth-normal saline in 5 per cent dextrose at the rate of 20 cubic centimeters per hour. For technical reasons however, it proved difficult to adhere to this standard of fluid requirement and rather less was administered. The catheter was withdrawn from the stomach at 3:00 p.m. on February 15, 1951 in order to administer a dilute feed of barium sulfate in milk. After x-ray screening it was replaced at 10:00 p.m. and about 37 cubic centimeters of barium and gastric contents were aspirated between 10:00 p.m. (Feb. 15, 1951) and 6:00 a.m. (Feb. 16, 1951). Screening after being given barium showed moderate dilatation of the stomach (Fig. 3). At 2 hours a large part of the barium had passed into the upper small bowel. In the lateral view however, the duodenum was seen well outlined and filled with barium (Fig. 4). An anteroposterior view taken at the end of 2½ hours demonstrated that there was still a considerable quantity of barium retained in the stomach and duodenum (Fig. 5). The roentgenographic findings were strongly suggestive of an incomplete but high intestinal obstruction and a provisional diagnosis of volvulus neonatorum was made.

On February 16, 1951 gastric suction was abandoned and feeding by mouth was tried again. Feeds consisting of 2 ounces of glucose saline were given at 2 hour intervals commencing at 11:00 a.m. She kept her feeds down successfully until evening. At 8:00 p.m. she vomited 8 ounces of pale green fluid. It was decided finally that the obstruction was sufficiently severe to warrant abdominal exploration.

Operation. The operation took place at about 9:00 p.m. The anesthetic was nitrous oxide, oxygen, and ether by use of an intratracheal tube. The abdomen was opened by means of a right upper paramedian incision. Immediately the peritoneum was incised a grossly distended stomach presented. In order to obtain satisfactory access to the peritoneal cavity it was necessary to decompress the stomach by esophageal catheterization. The pyloric end of the stomach was examined. No stricture or tumor was detected. The transverse colon and great omentum were retracted upward in order to obtain a view of the third portion of the duodenum. It was seen to be greatly distended and bulging downward and forward. The first 2 inches of the jejunum were also extremely distended. The distention ended abruptly at a point 2 to 3 inches below the duodenojejunal flexure.

Two factors were seen to be the cause of the high intestinal obstruction. Firstly, there was a well defined reflection of the peritoneum disposed in a fan-like manner lying at the root of the mesentery of the small intestine. This reflection or adventitious sheet of vascularized peritoneum was attached above along the anterior aspect of the first 2 or 3 inches of the jejunum. From this upper attachment it widened below and merged with the peritoneum of the posterior abdominal wall. The right edge of the fan was well defined and sharp. It was about 3 inches long and reached at its lower attachment the antimesenteric border of the terminal ileum about half an inch from the ileocecal junction. This edge therefore, corresponded approximately with what should be normally the root of the mesentery. The cecum was completely free and mobile. Although normally disposed anatomically immediately to the right of the midline it was suspended from the first few inches of the jejunum by this sharp edge of the accessory and abnormal peritoneal reflection. To the left of this edge, the fan-like sheet merged with the peritoneum of the posterior abdominal wall. The peritoneal reflection contained fine vessels accentuating the direction and disposition of the abnormality. The sharp right edge of the sheet was rendered tense by the weight of the cecum and marked narrowing of the first portion of the jejunum was caused at its upper attachment (Fig. 6). Secondly, the abnormal fixity of the first portion of the jejunum was responsible for a volvulus of the mobile jejunum immediately below. The weight of this free and mobile jejunum immediately following a fixed portion had resulted in an acute angulation. The gut below the fixed portion had fallen forward and to the left, producing an obstruction to the lumen (Fig. 6).

Division of the abnormal peritoneal reflection along the line of the left edge of the first 3 inches of the jejunum released the compression. Mobilization of the first portion of the jejunum was then effected easily by separation of filmy adhesions, after which the acute kinking of the jejunum below was corrected and showed no tendency to recur. The collapsed coils of jejunum below the angulation were seen to fill from above.

A third abnormality was also noted. There was present a short and strong fibrous adhesion approximating the right leaf of the mesentery of the small intestine about its center to the base of the transverse mesocolon. An attempt was made to divide this and to mobilize the mesentery but was given up when it was seen to contain a very large vein. Further to the left in a normal position the superior mesenteric vessels could be seen and palpated as they crossed the third portion of the duodenum and entered the mesentery (Fig. 6). This abnormal fixation did not seem to be responsible in any way for the patient's signs and symptoms.

Following operation, continuous gastric aspiration was continued and electrolyte balance was maintained by intravenous fifth-normal saline and 5 per cent dextrose, half strength plasma, and half strength Hartmann's solution. On the morning of February 18, 1951 oral feeding was commenced with 1 ounce

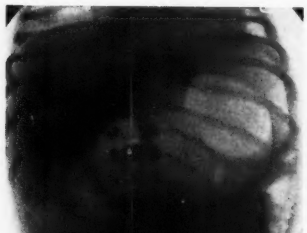

Fig. 1.

Fig. 2.

Fig. 3.

Fig. 4.

Fig. 1. Straight x-ray film of abdomen in supine position shows markedly distended stomach and duodenum filled with gas.

Fig. 2. Straight x-ray film in erect position shows fluid level which may be in the stomach.

Fig. 3. X-ray film of abdomen immediately after barium meal. Dilatation of stomach shown.

Fig. 4. Lateral view outlining stomach and duodenum. Some barium in small intestines.

Fig. 5. X-ray film of abdomen 2½ hours after barium meal. Barium still in stomach and lower end of esophagus. Some barium in the duodenum and a small amount in the small intestine.

Fig. 5.

of glucose saline at hourly intervals. This was increased to 2 ounces 2 hourly at 7:00 p.m. On February 20, 1951 oral feeding was continued with half cream National dried milk, 2 measures in 2½ ounces of water 3 hourly. Penicillin, 200,000 units in ½ cubic centimeter, was given every 6 hours on account of mild infection of the drip incision. This was discontinued on March 2, 1951. The patient was not pyrexial except during the first 24 hours (100.2 degrees F.) of the second admission to hospital (Feb. 14, 1951).

Normal bowel action gradually established itself during the days succeeding February 19, 1951.

On March 6, 1951 at 10:15 p.m. 3 attacks of twitching of the left arm and a squint of the left eye were observed. Each attack lasted about 10 minutes and at 5 minute intervals. She vomited after the attacks. No further convulsions took place while she was in hospital. The patient's weight on February 14, 1951 was 7 pounds 4½ ounces. There was slight loss in weight following operation but on March 3, 1951 she weighed 7 pounds 3 ounces.

She was discharged on March 17, 1951. The wound was healed, she was taking feeds satisfactorily and bowel action was normal. Her weight on discharge was 8 pounds 2 ounces. Following discharge from hospital progress was satisfactory as far as the abdominal condition was concerned and she was seen at monthly intervals for 9 months.

There has been, however, the development of another condition which is unlikely to be in any way associated with her intestinal obstruction—except in so far as when there is one congenital anomaly others may occur elsewhere. Six weeks after the operation her mother noticed a recurrence of the twitching of the left arm, leg, and left eyelid. This

occurred several times and on examination she was discovered to be suffering from a left-sided spastic hemiparesis. A stereoscopic roentgenogram of the skull showed an irregular shadow resembling calcification over the right parietal region. The patient was referred to a medical colleague. The convulsion which occurred on March 6, 1951 was clearly part of this clinical picture. It is unlikely that this condition is in any way related to the intestinal abnormalities.

CASE 2. The patient, P. A., female, was born on June 26, 1951. She was admitted to Alder Hey Children's Hospital on July 17, 1951 at the age of 3 weeks. It was the mother's first pregnancy and it was normal. Delivery took place at home and at full term. Labor was prolonged but the patient appeared healthy at birth. Birth weight was 8 pounds 10½ ounces. The patient was breast fed for 13 days. This was then changed for maternal reasons to Truefood. Her weight on admission to hospital was 8 pounds 5½ ounces, having lost 5 ounces in the first 3 weeks of life. Both mother and father were healthy. There was no tuberculosis in the family. This was their first child. The patient came from a good middle class family.

Feeds were always taken readily (2½ to 3 ozs. every 3 hours), but intermittent vomiting occurred from birth. Not every feed was returned and sometimes 2 or 3 days would elapse without vomiting. The vomited material was bile-stained. The bowels were opened daily but there was a tendency to constipation. The stools appeared to be quite normal, containing no blood or mucus. At times she was seen to draw up her knees as if she was having some abdominal pain. On examination, her general condition was good. There were no signs of dehydration and no obvious congenital anomalies. The heart, chest, and central nervous system showed no abnormal physical signs. Abdominal examination was normal.

A roentgenographic examination after a feed of barium sulfate diluted with milk gave the following findings: "The opaque solution passed normally through the pharynx and esophagus into the stomach. The stomach was normal in size, shape, and position. Emptying took place slowly. There was no evidence of organic disease of the stomach. There was gross dilatation of the first and second parts of the duodenum and the proximal portions of the third part, with stasis in these regions." These findings are shown in films taken at intervals following the swallowing of the opaque meal. Films were taken immediately after the meal, after ½ hour, after 1½ hours, and finally at 6 hours (Figs. 7 and 8). Some of the solution passed into the jejunum and colon. The appearance pointed to incomplete duodenal obstruction, probably due to a volvulus associated with malrotation of the intestine.

She was given Truefood 3 ounces every 2½ hours, and vomiting did not occur. Preparations were made for a laparotomy. An intravenous drip was set up of fifth-normal saline and 5 per cent dextrose and allowed to run at approximately 50 cubic centimeters per hour. A small catheter was passed into the stomach and gastric lavage carried out, using normal saline, 1 hour before operation. The catheter was left in situ for the purpose of gastric aspiration. Atropine, 1/200 grain, was given half an hour before operation.

Fig. 6. Operative findings. Abnormal sheet of peritoneum attached above to first part of jejunum and below the cecum (see text). Torsion of first part of jejunum. Adhesion of mesentery to transverse mesocolon.

Operation (Fig. 9). The anesthetic was endotracheal gas, oxygen, and ether. A liberal right paramedian incision was made. A good view of the peritoneal cavity was obtained. The stomach was normal in appearance. The transverse colon, however, lay in close proximity to the greater curvature and the absence of great omentum was noted. The cecum and appendix were situated high in the abdominal cavity and near the midline. There was a well defined sheet of peritoneum (Ladd's membrane) attached to the cecum and hepatic flexure and stretching across the second part of the duodenum, to be attached on the right side to the peritoneum of the posterior abdominal wall immediately to the right of the second or descending portion of the duodenum. This sheet was divided between forceps. The second portion of the duodenum was seen to be markedly distended. There was no posterior fixation of the cecum and there was a very short ascending

Fig. 7.

Fig. 8.

Fig. 7. X-ray film of abdomen half an hour after meal of barium. Barium seen retained in stomach and duodenum both of which are distended. Some barium in the small intestines.

Fig. 8. X-ray film of abdomen 1½ hours after meal of barium. Duodenum outlined. Some barium in small intestines.

colon also lacking posterior fixation and joining the transverse colon at an acute angle corresponding to the hepatic flexure.

Attention was turned to the small intestine. It was seen that the whole of the small intestine, the cecum, the short ascending colon, and the transverse colon were suspended from the posterior abdominal wall by a common mesentery. This mesentery was fan-shaped, having a narrow upper attachment at the apex of the fan to the posterior abdominal wall, corresponding to the position of the superior mesenteric vessels at the lower margin of the pancreas. The normal fixation of the mesentery of the small intestine across the posterior abdominal wall from right to left and above downward was absent. The ileocecal angle however was fixed secondarily to the posterior abdominal wall. In this situation there was a deficiency in the common mesentery. A loop of terminal ileum immediately proximal to the ileocecal junction was herniated through the hiatus from above downward. To obtain a satisfactory view it was necessary to lift up the cecum and draw it toward the upper abdomen. The loop was about 2 inches in length and fixed to the posterior abdominal wall by filmy adhesions which represented a kind of hernial sac attached around the margins of the deficiency. The adhesions were divided and the loop of ileum was released and withdrawn through the deficiency in the mesentery. The margins of the aperture were drawn together and sutured with fine catgut. The rest of the intestines had rotated clockwise through 180 degrees on the narrow pedicle.

When the rotation was corrected a strong adventitial band of peritoneum was clearly seen crossing obliquely downward and to the left, attached above on the right side of the duodenojejunal flexure and below on the posterior abdominal wall in the renal region. This strong band had almost completely obstructed the commencement of the jejunum, immediately below the duodenojejunal flexure. As soon as it was cut, the distended third part of the duodenum and duodenojejunal flexure released its contents into the upper jejunum, which was seen to fill up. The abdomen was closed in the normal way.

Postoperative progress. Oral feeding was commenced 1 hour after operation. Half-hourly feeds of 1 dram of half-strength saline were given for 2 hours, then expressed breast milk, 1 dram at first hourly. Feeds were augmented gradually and at the end of 12 hours 1 ounce of expressed breast milk was being given hourly, and at the end of 24 hours following operation, she was taking 2½ ounces of Truefood every 3 hours. Distaquaine, ½ cubic centimeter twice a day, was administered as a precautionary measure. The intravenous glucose saline was stopped at the end of 24 hours. Her weight on July 23, 1951 was 8 pounds 11 ounces. No further vomiting occurred and bowel action took place normally. She subsequently showed a tendency to be constipated and she was kept under observation for some weeks. There was no further vomiting and the constipation was easily corrected. Her weight on August 20, 1951 was 8 pounds 13½ ounces.

CASE 3. The patient, M.P., female, was born at 2:40 p.m. on December 10, 1951. She was transferred to Alder Hey Children's Hospital, Liverpool, 24 hours later on December 11, 1951. Her birth was by vertex delivery. There was difficulty in delivering

the trunk. This was found to be due to abdominal distention. She was cyanosed at birth and vomited greenish fluid immediately. It was the mother's third pregnancy. The first was normal; the second terminated in a miscarriage at 3 months in 1950. The last pregnancy was normal. The father was alive and well. The previous child was also alive and well.

Vomiting commenced as soon as she was put to the breast. A few hours after birth a soft rubber catheter was passed into the stomach and aspirations carried out at 15 minute intervals. Nothing was given by mouth. She was nursed in an oxygen tent. A catheter inserted into the rectum when she was 6 hours old obtained no flatus but a small quantity of blood-stained brownish fluid.

Her weight was 5 pounds 14½ ounces. There was no evidence of dehydration and her temperature was normal. The abdomen was distended and tense. No bowel sounds were heard. Rectal examination showed patent anus and good sphincter. Some brownish staining was observed at the anus.

A straight roentgenogram of the abdomen demonstrated diffuse gas shadows, but no fluid levels. Lipiodol was instilled into the stomach by means of a soft rubber catheter. This was not retained in the stomach and passed through the duodenum in the normal time. Distended coils of intestine containing lipiodol were visualized after 2 hours and a provisional diagnosis of atresia at some point in the intestine was made (Fig. 10).

The hemoglobin was 143 per cent. Blood urea 54 milligrams per cent and sodium chloride 626 milligrams per cent.

Preparations were made for laparotomy. An intravenous drip of fifth-normal saline and 5 per cent dextrose was established at the ankle and allowed to flow at 10 to 15 cubic centimeters per hour. Preoperative atropine, grain 1/400, was given. Operation was performed at 11:00 p.m. on December 11, 1951, approximately 32 hours after delivery. An endotracheal tube was inserted and gas, oxygen, and ether were given. A right paramedian incision was made. There was general peritonitis, and meconium was free in the peritoneal cavity. The jejunum and ileum were grossly distended. The cecum was identified. Cecum and colon were pencil-like in diameter. The distended ileum was traced down to the ileocecal region. A large circular defect about 2 inches in diameter in the mesentery at the ileocecal angle was found. The defect was bounded by a sharp edge. The terminal ileum had herniated through the hiatus. The proximal end of the prolapsed loop of gut was sharply angulated over the edge of the hiatus. The herniated gut was a dark plum color, grossly distended, and occupied the right iliac fossa lying against the posterior abdominal wall. The distal end of the herniated loop of ileum ended as a blind sac. A fibrous cord about 1 inch long, which was attached to the blind end returned through the hiatus over its sharp edge and became continuous with a small stump about 1 inch long of terminal ileum opening into the cecum (Fig. 11). The free meconium

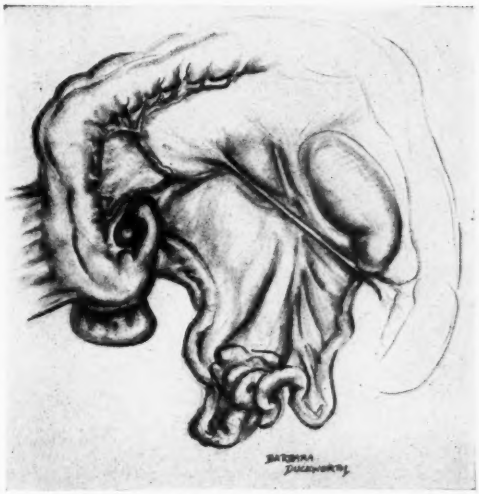

Fig. 9. Operation findings demonstrating: (1) well defined Ladd's membrane, (2) herniation of loop of small intestine through hiatus in mesentery, (3) abnormal band constricting jejunum, (4) small intestine and colon having common mesentery without normal fixation to posterior abdominal wall. A volvulus of the midgut had also occurred and had been corrected at operation.

in the peritoneum was evidence that there had been a perforation of the gut at some point although the exact site could not be discovered. A resection of the herniated gut was carried out—about 12 inches altogether. A large rubber catheter (the end having been cut off) was tied into the open end of ileum which was brought to the surface. The abdominal wall was sutured in layers round this projecting portion of terminal ileum.

Examination of the operation specimen showed evidence of a minute canal in the center of the fibrous cord attached to the apparently blind ileal sac. The later postmortem findings strengthened the view that this was a case of severe stenosis of the ileum and not as was at first thought complete atresia of a portion of ileum.

Blood was given during the operation and immediately after returning to the ward—60 cubic centimeters altogether. Gastric aspirations were continued, but only small quantities of fluid were obtained (½ c.c. half hourly). Fluid and electrolyte replacement were maintained by intravenous drip from midnight December 11, 1951 until the morning of December 14, 1951. An average of 300 cubic centimeters in 24 hours was given consisting of fifth-normal saline and 5 per cent dextrose, and Darrow's solution. Oral feeding was commenced at 9:00 p.m. December 12, 1951 twenty-four hours following operation, 1 dram 2 hourly, and increased gradually to 2 drams 2 hourly on the evening of December 13, 1951.

Fig. 10. Lipiodol retained in distended coils of small intestine 2 hours after instillation into stomach.

A 10 per cent solution of pancreatin was run into the enterostomy following operation each half hour in an attempt to dissolve the inspissated meconium. Five cubic centimeters of pancreatin were also run into the stomach via the catheter at 8:00 p.m. December 12, 1951 and 4:00 a.m. December 13, 1951. Very little fecal matter escaped from the enterostomy. Streptomycin, 60 milligrams twice a day, was given and distaquaine penicillin ¼ cubic centimeter twice a day. She was nursed in an oxygen tent.

The blood chemistry showed no significant alteration. On December 12, 1951 blood urea was 49 milligrams per cent, serum chloride 572 milligrams per cent, serum protein 4.5 grams per cent, hemoglobin 119 per cent. On December 13, 1951 blood urea was 34 milligrams per cent and serum chloride 545 milligrams per cent.

On December 14, 1951 at about 9:30 a.m. the patient vomited greenish fluid. Half an hour later she collapsed and died apparently from circulatory failure.

Autopsy findings. A summary of only the main autopsy findings is given. There was slight edema of the legs and vulva. The lungs were slightly edematous and there was a little free fluid in each pleural cavity. The peritoneal cavity was completely obliterated by thick green meconium—all the coils of the intestine were adherent to one another. The stomach was filled with tenacious dark green mucoid material, the ileum with extremely thick meconium—only the last few centimeters at the ileostomy were empty. The cecum and 3 centimeters of terminal ileum lay in the right iliac fossa. They appeared to be free and mesentery was almost nonexistent. The 3 centimeters of terminal ileum had a rounded proximal end on the peritoneal surface of which was a small white nodule. This might represent part of the band cut at operation. The large gut was very narrow in diameter and contained small quantities of inspissated meconium. In the small portion of the terminal ileum it formed a hard cast.

There was no obvious evidence as to the final cause of death. It was thought however that potassium deficiency may have been an important factor. However, there was no doubt of the profound toxemia resulting from the peritonitis. The presence of meconium in the distal portion of the alimentary tract would strongly suggest that the condition was probably a stenosis rather than atresia unless one presumed the lumen of the ileum to have been open throughout its length at one time in fetal life and to have undergone atresic change later. It is more than probable that the peritonitis was caused by leak from the over distended gut probably as a result of the difficult delivery.

DISCUSSION

In order to appreciate the significance of the operation findings in these cases of malrotation and nonrotation of the midgut, one must understand the early embryology. The processes involved have been carefully worked out by Dott (1923). At about the fourth week of intrauterine life the midgut is herniated through the anterior abdominal wall at the umbilicus. During the tenth week it returns to the peritoneal cavity from the hernial sac. The process of returning is an orderly one and it is at this stage that the final disposition of various portions of the midgut is established. Normally, the proximal loops re-enter the abdomen first and are directed posteriorly and downward behind the superior mesenteric artery. The last to re-enter is the cecum. If, however, this process of rotation does not occur, the whole of the midgut is returned to the peritoneal cavity en masse. This results in an infantile disposition of the viscera, and the normal posterior fixation of cecum and ascending colon does not occur. The whole midgut is suspended from the posterior abdominal wall by a mesentery which has very limited vertebral attachment. The cecum is in the midline or toward the left of the abdomen and the ileum opens into its right aspect.

The portion of the colon which would normally be called transverse anatomically, runs downward on the left side into the descending colon and sigmoid. This large mass of intestines and colon suspended from the posterior abdominal wall by a narrow pedicle and without the normal parietal fixations easily undergoes torsion. When torsion occurs the narrow mesentery containing the superior mesenteric vessels is twisted like a corkscrew and compresses the third portion of the duodenum. Many authorities have described this condition in infancy and childhood. Among these are Foucar (1933), Raymond and Dragstedt (1931), Gardner and Hart (1934), Wakefield and Moore (1936), King (1937), McIntosh and Donovan (1939), Ladd and Gross (1941), Quilliam (1946), Embleton and Jones (1946), Markby (1946), and Wright (1947).

There are two forms of intestinal obstruction produced by this mechanism. There is the constriction of the third portion of the duodenum by the root of the mesentery and also the partially "closed loop" obstruction of the volvulus itself. In these cases the main symptoms and signs exhibited by the patient are predominantly caused by the duodenal obstructions. In spite of the severity in the twist of the mesentery, the blood supply of the intestines is not seriously impaired. There may be venous engorgement, but gangrene is rare. Moreover the obstruction is not closed below since feces or altered blood may be passed per rectum.

The operation findings are rarely as simple as the description given would suggest—namely, a duodenal obstruction and twisted coils of intestine. If that were so the condition would be relieved merely by untwisting the mesentery. It is most important to realize that simple untwisting of the volvulus does not necessarily give complete relief to the condition. Other congenital abnormalities may be present and indeed this is the rule rather than the exception. There are usually adventitious peritoneal bands and reflections, which unless divided prevent relief of the obstruction. Ladd (1941) has emphasized the presence in many of these cases of a sheet of peritoneum passing from right to left across the second part of the duodenum and attached

Fig. 11. Operation findings: Case M. P. Hiatus in mesentery and herniated terminal ileum.

to the cecum as it lies in its abnormal position in the epigastric region. Other authorities have noticed adventitial bands and adhesions which required division. Judd and White (1939), mention a patient aged 19 years who, from the age of 2 years, suffered from attacks of generalized abdominal pain and vomiting every 2 or 3 weeks. At operation the patient was found to have obstruction at the duodenojejunal flexure caused by an abnormal band 7.5 centimeters wide, extending from the root of the mesentery across the duodenojejunal flexure and becoming continuous with the posterior leaf of the transverse mesocolon. Division of the band relieved the patient of his obstruction. Waugh (1928), describes a case of a boy of 7½ years who had constriction of the second part of the duodenum by a cysticocolic membrane, passing over the second part of the duodenum to end at the hepatic flexure of the colon. In the author's case (1951), of duodenal ileus caused by volvulus of the midgut in a female aged 2½ years, a sheet of adhesions attached the right aspect of the first few inches of jejunum to the posterior abdominal wall and caused a constriction of this portion of the intestine (15). The volvulus was easily recognized and corrected. The sheet of adhesions might easily have been

missed. Indeed, although most of the sheet was divided at the first operation, a second exploration was required to complete the division. After this the patient made a good recovery.

Other abnormalities such as atresia or stenosis of other portions of the intestines may also be present and require correction. These factors must be borne in mind when operating upon one of these patients presenting with volvulus neonatorum.

When dealing with one of these cases in which there is failure of posterior fixation of the midgut and a tendency to volvulus the two sites of particular importance in looking for bands and other congenital anomalies are the first portion of the jejunum and the ileocecal region and it is reasonable to associate these anomalies with the mechanism of re-entry of the midgut to the general peritoneal cavity. It would seem as if the normal process of the midgut re-entering the peritoneum may be disturbed before the final disposition as seen in the normal is completed. The prearterial loop of gut starts quite normally to re-enter behind the mesenteric artery and then it is as if mass re-entry occurs before the remainder of the postarterial gut has been drawn in. Following this the first portion of the jejunum immediately distal to the duodenojejunal flexure becomes fixed to the posterior abdominal wall instead of, as it normally does, lying free with a mesentery. In the normal state, a more thorough re-entry of the prearterial gut behind the mesenteric artery would theoretically give greater freedom and mobility to this part of the gut and it would be the mesentery which would attach itself to the posterior abdominal wall in the normal position of the root of the mesentery. It would appear that these pathological congenital adhesions and fixations in the region of the duodenojejunal flexure are the result of incomplete postarterial re-entry into the peritoneum at an early stage in the closure of the physiological hernia. The freely mobile unattached cecum and ascending colon (if one exists) cannot be looked upon as abnormal. The acquisition of posterior fixation and its final position in the right iliac fossa take place at a late stage in the evolution of the midgut and it is usual at birth and in infancy to find the cecum and ascending colon unattached and occupying a position in the right lumbar or right subcostal region of the abdomen.

It is natural to expect defects in the mesentery or atresia of the gut to occur in a situation where, in the event of abnormal stress, the blood supply is precarious. The ileocecal region is the last portion of the gut to re-enter the abdomen and, although in the direct line of the superior mesenteric axis, is placed at the least advantage in the supply of blood along anastomotic pathways.

As already stated, the 3 patients described had one feature common to all, namely, inadequate and incomplete fixation of the midgut and its mesentery to the posterior abdominal wall. Volvulus in one manner or another had occurred in all 3.

The first, P.I., had a free unattached mesentery, no twist of the mesentery, no duodenal compression but again an abnormal fixation of the first 3 inches of the jejunum and a curious constricting kink in this region.

The second, P.A., demonstrated a free unattached mesentery, volvulus of the small intestines through 180 degrees, no duodenal compression, constriction of the upper jejunum by a strong fibrous band crossing it obliquely from above downward and from right to left from the underleaf of the transverse mesocolon to the posterior abdominal wall, an internal herniation of the terminal ileum through a defect in the mesentery near the ileocecal angle, and finally a well defined Ladd's membrane which was not an immediate cause of intestinal obstruction.

The third case, M.P., showed a free, inadequately attached mesentery (the cecum and ascending colon had no posterior fixation to the posterior abdominal wall), a herniation through a large defect in the mesentery at the ileocecal angle and finally atresia or stenosis of the terminal ileum.

Diagnosis of these cases is influenced by the severity of the obstruction. Thus cases may be presented to the clinician and recognized in the first few days or weeks of life. If there is an absolute obstruction, surgical relief will be required. However, if the obstruction is reversible (e.g., the untwisting of a volvulus),

an incorrect diagnosis of "cyclical vomiting" or "feeding error" may be made and symptoms may recur months or even years later. Miller and Gage (1930) discussed the late onset of duodenal obstruction in later life when visceroptosis is superimposed on a congenital tendency to arteriomesenteric compression.

When vomiting occurs in the early days or weeks, it is necessary at first to eliminate the possibility of feeding errors. The character of the vomiting and the type of vomitus (bile-stained or otherwise), the passage of stools or constipation, the presence of visible peristalsis and the presence or absence of a palpable tumor are all taken into account. The presence or absence of bile in the vomit is of particular importance. If there is a condition of duodenal atresia, the usual site of the obstruction occurs in the second portion about the level of the ampulla of Vater. Bile is still present in the vomit since the pancreas is drained by an accessory duct opening into the duodenum above.

The most important diagnostic aid is roentgenography. The gas distended stomach and duodenum may be visualized in a straight x-ray film. The absence of gas in the intestines below the duodenum is strong evidence of a complete obstruction of the duodenum. Partial obstruction will allow the intestines to contain gas shadows. The presence of a fluid level shown in the roentgenogram indicates a dilated loop of intestine containing fluid as well as gas. It is important to have roentgenograms taken with the patient held in an erect position in addition to lying supine.

A meal of barium diluted with milk may be administered and serves to confirm the findings observed by a straight roentgenogram. The presence of barium in the stomach after 2 hours indicates marked delay in emptying. The administration of barium is not devoid of danger. A partial obstruction may be made complete and there is always the possibility of aspiration of the solution into the lungs. To minimize the risks, the barium should be well diluted and, after the roentgenograms have been taken, it should be aspirated from the stomach.

In the differential diagnosis, other conditions may produce a very similar picture to the one we have been describing. Among these are congenital atresia of stenosis of the duodenum, enlarged glands in the mesentery compressing the duodenum, obstruction by tumor or an abnormality of the pancreas which may encircle a portion of the duodenum. In an older patient, cicatrization from peptic ulceration has to be considered (Miller 1936).

Treatment of these cases is essentially a surgical problem. Not all individuals having the congenital abnormality of the mesentery which predisposes to the occurrence of volvulus present with symptoms. Dott (1923) reviewed 48 cases in 1923, five of which were personal cases. He pointed out that symptoms had occurred in only 13 of these. A person may go through life with the condition unrecognized or if found it is incidental.

Jones and Morton (1938), have expressed the view that in some cases there are periodic attacks superimposed on a background of "marginal disturbance." The marginal disturbance is partial duodenal obstruction and the superimposed attacks are caused by the occurrence of volvulus. In their opinion the patient may recover spontaneously from an attack after vomiting.

Ladd (1941), on the other hand, emphasizes that the onset of symptoms occurs early. In a series of 44 cases, 26 were seen within the first 3 weeks of life.

From the various accounts it would seem to indicate that there is a great variation in the age of onset, the suddenness and the urgency of the treatment. This is explained by the complexity of the operation findings. Where there is this congenital anomaly predisposing to volvulus, it is probable that other congenital abnormalities are present in addition, for example, atresia, stenosis, internal herniation, and adventitious bands.

Acute intestinal obstruction may occur therefore at any time and the volvulus is usually only part of the picture at operation. The surgical procedure must be dictated by the findings in any individual case. This has been discussed in a previous paper by the author (15). Reduction of the volvulus is performed. Adventitious bands and adhesions and other congenital abnormalities are looked for and corrected. It is generally agreed that

there is no need to perform a fixation of the cecum in the right iliac fossa to prevent a recurrence of the volvulus. I have not read any accounts of recurrence of the volvulus requiring a second exploration of the abdomen, and this in itself seems to be strong evidence to support the view that the volvulus is probably not the primary lesion, but rather it develops secondarily after obstruction due to bands or other congenital abnormalities.

SUMMARY

Three cases of volvulus neonatorum have been described. In the first the symptoms and signs commenced at 4 days, in the second at 3 weeks, and in the third from birth. In the first 2 cases relief was obtained only by operation. The third patient died.

The subject of volvulus neonatorum has been discussed.

The problem of diagnosis is considered. Emphasis is laid on the importance of recognizing the condition when vomiting and feeding difficulties occur in early infancy. The symptoms may be sufficiently severe to necessitate early operative relief. In some of the milder cases, spontaneous regression of symptoms may take place but the congenital anomaly remains and at a later period—late childhood and adult life may account for obscure dyspepsia and abdominal pain.

REFERENCES

1. Dott, N. M. Anomalies of intestinal rotation; their embryology and surgical aspects. Brit. J. Surg., 1923, 11: 251.
2. Embleton, D. M., and Jones, P. Volvulus of small bowel, with report of case treated by resection with recovery. Med. J. Australia, 1946, 1: 144–145.
3. Foucar, H. O. Intermittent duodenal obstruction in children. Med. Clin. N. America, 1923, 7: 81–87.
4. Gardner, C. E., Jr., and Hart, D. Anomalies of intestinal rotation as a cause of intestinal obstruction; report of two personal observations; review of 103 reported cases. Arch. Surg., 1934, 29: 942.
5. Jones, T. B., and Morton, J. J. Congenital malformation of the intestines in children. Am. J. Surg., 1938, 39: 382.
6. Judd, E. S., and White, R. B. Congenital anomalies of duodenum with obstruction at duodenojejunal angle. Ann. Surg., 1929, 89: 1–5.
7. King, E. S. J. Two uncommon forms of intestinal obstruction occurring consecutively; compound volvulus and retroposition of the transverse colon. Brit. J. Surg., 1937, 24: 817.
8. Ladd, W. E., and Gross, R. E. Abdominal Surgery of Infancy and Childhood. Philadelphia: W. B. Saunders & Co., 1941 and 1947.
9. Markby, E. C. P. Derangement of midgut rotation producing volvulus; report of 2 cases. Brit. J. Surg., 1946, 34: 80–83.
10. McIntosh, R., and Donovan, E. J. Disturbances of rotation of the intestinal tract; clinical picture based on observations of 20 cases. Am. J. Dis. Child., 1939, 57: 116.
11. Miller, R. Arch. Dis. Childh., Lond., 1936, 5: 133.
12. Miller, R., and Gage, R. C. Gastromegaly and chronic duodenal ileus in children. Arch. Dis. Childh., Lond., 1930, 5: 83.
13. Quilliam, T. A. Volvulus of small intestine. Brit. M. J., 1946, 1: 434.
14. Raymond, H. E., and Dragstedt, L. R. Anomalies of intestinal rotation; a review of the literature with report of 2 cases. Surg. Gyn. Obst., 1931, 53: 316.
15. Spencer, R. Brit. J. Surg., 1951, 39: 154.
16. Wakefield, W. G., and Mayo, C. W. Intestinal obstruction produced by mesenteric bands in association with failure of intestinal rotation. Arch Surg., 1936, 33: 47.
17. Waugh, G. E. Clinical aspect of congenital mesenteric malformation in children; president's address. Proc. R. Soc. M., London. (Sect. Dis. Child.), 1928, 21: 79–85.
18. Wright, R. D. B. Volvulus in 48 hour old baby; operation; recovery. Brit. M. J., 1947, 2: 773.

CARCINOMA ARISING IN THE SCARS OF THERMAL BURNS

With Special Reference to the Influence of the Age at Burn on the Length of the Induction Period

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CARCINOMA of the skin is one of the common malignant disorders of man. Although it was one of the disease processes that was recognized many centuries ago, it was not until Percivall Pott drew attention to the importance of coal soot as a stimulus to its inception that a specific external chemical was proposed as an etiological factor. In subsequent centuries, the search for carcinogenic agents waxed intense, but when a few decades ago it became apparent that there were many potential etiological factors for this neoplasm as well as others, the search was broadened with the hope of explaining the origin of the process. Our present understanding of the complexity of the situation, particularly in experimental animals, is due in large measure to the efforts of the group at the Barnard Free Skin and Cancer Hospital that, over a period of years, has reported extensive studies on variations in the chemical constituents of the skin of mice undergoing malignant change from carcinogenic stimulation as well as the importance of elastic fibers, collagen, sebum, and other associated factors.

The experimental study of carcinogens has shown that a significant period of time must elapse between the first exposure to the agent and the origin of the neoplasm. In most instances, this time interval consumes a considerable proportion of the life span of the experimental subject. The significance of the time element as well as the inherent susceptibility of the host in carcinogenesis has been emphasized by Cramer who has suggested that it is as applicable to the human individual as to the laboratory animal. A large variety of chemical agents have been implicated in the genesis of human cancer, and we have every reason to believe that a human patient, as is generally true of the laboratory animal, must be exposed to the carcinogenic material for a period proportionately equal to a similar period in an animal.

A type of clinical carcinoma that illustrates the relationship between the time element and tissue susceptibility is that which arises in the scars of thermal burns. It is a well recognized clinical phenomenon. Although its pathological characteristics, clinical course, and therapeutic management have been thoroughly described, there has been wide speculation as to methods of its origin. Treves and Pack postulated that the scar from a burn is a poorly vascularized structure and is susceptible to ulceration because of its poor nutrition; that the inelasticity of the scar permits the epithelium on it to be injured more easily than that of normal skin; that the regenerating epithelium becomes progressively inferior; and that the persistent stimulation to the marginal epithelium for repeated growth leads to a loss of tissue restraint and carcinoma. They further proposed that in acute burn scar cancer, tissue toxins were released by autolysis and heterolysis from the burn scar that might act as direct carcinogenic agents. Hueper believes that this latter concept gains in probability by the fact that during heat destruction of organic matter, substances having carcinogenic qualities may be produced and be included in the regenerating tissue, thus remaining in prolonged contact with the proliferating epidermal cells and ultimately causing their carcinomatous transformation; and that it is supported by the reported demonstration of necrotic charred matter within the tissues of the burn

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scar. Roffo and Gandolfo (13) contended that burn scar carcinomas appeared to originate from misplaced epithelial cell groups. Kennaway, according to Hueper, has demonstrated that human skin subjected to destructive distillation yields a tarry material possessing carcinogenic properties.

Such proposals are theoretical considerations, and as far as we are aware none has been corroborated clinically. Furthermore, efforts to produce carcinoma in burns of the skin of experimental animals have not been notably successful. Bang produced carcinoma in the skin of 2 mice from burns with a hot glass rod. Simpson in a study in mice of the effects of a burn of skin that was prepared by "inactive" solutions of methylcholanthrene in lanolin with a hot glass rod found that in two groups of animals malignant tumors appeared in 42 per cent and 65 per cent, respectively. The average latent period was 7 months. We are not aware that the observations of these authors have been verified by others and are forced to conclude that neither clinical nor experimental investigations have yielded sound explanations for the origin of this type of malignant neoplasm.

It is interesting that this should be true for it would seem that a patient with the wound and subsequent complication of a burn scar carcinoma would offer an opportunity for the study of the influence of potential factors of exposure and susceptibility to cancer in the human subject. The source of the heat causing the burn and the date of the trauma are known; the date of the origin of the neoplastic process can be determined within reasonable limits; the occupation and environment of the patient in the intervening years can be ascertained; and the nature of the chemicals used in the treatment of the ulcer elicited. These wounds usually heal only after prolonged periods of ulceration, or are ulcerated again later in life for lengthy periods of time before the diagnosis of carcinoma is finally established, thus offering opportunities for exposure of granulating surfaces and proliferating epithelium to the hazards of potential environmental carcinogenic agents such as occupational chemicals, sunlight, local trauma, and others.

The present investigation was undertaken with the hope of obtaining further information on factors, environmental and inherent, that could be of influence in the origin of carcinoma in the scars of thermal burns and was stimulated by the study of a number of patients with this complication of a burn scar seen at the Indiana University Medical Center. The wide variations in the latent period between the time of the burn and the diagnosis of carcinoma, the variation in the ages of the patients when carcinoma became established, the intermittent ulceration and healing of the scar, the types of medicaments that were used to promote healing of the original burn and the recurrent ulcers, and the many different occupations of the patients were impressive.

The material for the report consists of the 11 patients seen at this center and 82 of those recorded in the literature. Since we were particularly interested in an analysis of the relationship, or possible influence, of the age at the time of the burn on the length of the induction period before carcinoma became established, no case has been included unless both the ages at the time of the burn and at the time the diagnosis of carcinoma was made were recorded. The first age was definite in all cases included herein. The latter was not because of the uncertainty that arose from the fact that continuous ulceration was present for varying periods before the diagnosis of carcinoma in the scar could be established. For reasons that will be discussed later, it was decided to establish empirically the age at cancer as the age when the diagnosis was made rather than to try to interpret from the various reports the age at origin of the process.

Other reasons for not including cases that had been reported in the literature were the recorded use of x-ray or radium therapy to promote healing of the burn ulcer, and the presence of significant abnormalities of the skin in the burn area, prior to the burn.

CASE REPORTS

The following case summaries are of the patients seen at the Indiana University Medical Center that met the above criteria.

CASE 1. I.S., a 56 year old white man, was admitted on February 13, 1933, complaining of a sore

on the right shoulder where he had been burned 20 years previously with molten metal. The burn had healed slowly and remained healed until 2 years before admission when he bruised the scar, and an ulcer developed in it. Five months before admission a skin graft was applied to the ulcer, but it did not take. Examination revealed the presence of an ulcer on the right shoulder measuring 3½ by 3 inches in size. Regional lymph node enlargement was not noted. The area was excised and a pedicle graft was placed in the defect. The operative wound healed well, but on June 26, 1933, a recurrence was noted at the tip of the shoulder. It was excised. Another recurrence appeared in August, 1934, but the patient refused to come into the hospital for further treatment and died with cancer on June 13, 1936.

The pathological diagnosis was squamous cell carcinoma.

CASE 2. B.C., a 56 year old white man, was admitted on November 23, 1933, complaining of an ulcer on the left leg just above the ankle. Twenty-six years previously the leg was burned with hot calcium water. The wound did not heal for 10 years. A few years later the scar ulcerated following trauma to it and healed with great difficulty. One year previous to admission, the scarred area became ulcerated again, and 6 months before admission, the ulcer began to enlarge. Examination revealed the presence of a scar on the left leg extending from the knee to the sole of the foot. Located in it at a level just above the ankle there was an ulcer that nearly encircled the leg. Femoral and inguinal lymph node enlargement was not described. A leg amputation was done on November 29, 1933. In 1938, the patient developed a squamous cell carcinoma of the lip that was treated elsewhere by surgical excision. He died on December 6, 1948, without evidence of residual carcinoma.

The pathological diagnosis was squamous cell carcinoma.

CASE 3. C.D., a 52 year old white man, was admitted on October 20, 1939, complaining of an ulcer on the left cheek. He had received a burn of the skin in this region 7 years before admission. Fifteen months prior to admission he cut this burn scar while shaving, and the wound did not heal. An ulcer appeared and enlarged slowly. Examination revealed the presence of a scar on the left cheek beneath the left eye, lateral to the nose. In its inferior border there was an ulcer, 1 by 2 centimeters in size. Regional lymph node enlargement was not noted. The ulcerated area was excised. The patient died of causes not related to the carcinoma on March 31, 1942. There was no evidence of recurrent disease.

The pathological diagnosis was basal cell carcinoma.

CASE 4. O.H., a 37 year old white man, was admitted on April 4, 1943, complaining of a scarred area on the scalp. When he was 3 years old, he fell into a fire and received a severe burn of his scalp. He did not know the duration of time that elapsed until the burn healed. Approximately 5½ years before his hospitalization, a small ulcer appeared in the scar and enlarged steadily. Examination revealed a fungating lesion which involved almost the entire posterior half of the scalp. Bilateral cervical lymph node enlargement was present. Roentgenograms of the skull showed extensive destruction of both tables of the calvarium in the right parietal and occipital regions. The patient was not accepted for treatment and died of his disease on July 31, 1943.

The pathological diagnosis of the biopsy was squamous cell carcinoma, grade 2.

CASE 5. R.A., a 41 year old woman, was admitted on April 23, 1943, complaining of an ulcer on the posterior scalp. When she was 16 months of age, she fell into a fire and received a severe burn in this region. She did not remember the length of time that transpired before healing of the burn was complete, but for the 25 years prior to admission continuous ulceration of the scar was present. Examination revealed the presence of an ulcer on the posterior scalp that measured 6 inches in diameter. The involved area on the scalp was excised. The outer table of the calvarium was removed, and skin grafts were applied to the defect. She later developed metastatic disease bilaterally in the cervical lymph nodes as well as recurrent disease of the scalp. These recurrences were treated with x-ray therapy without success, and she died with carcinoma on January 20, 1945.

The pathological diagnosis was squamous cell carcinoma, grade 2.

CASE 6. C.S., a 60 year old white man, was admitted on June 4, 1943, complaining of an ulcer on the scalp. When he was 7 months of age, he received a severe burn of the scalp that did not heal until he was 5 years old. Throughout his life there had been intermittent ulceration of the scar. An ulcer appeared 2 years prior to admission and slowly enlarged. Upon examination a fungating tumor mass was present on the left side of the scalp that measured 2 inches in diameter. Regional lymph node enlargement was not described. The lesion of the scalp was excised, and the outer table of the calvarium was fulgurated where it was involved by carcinoma. The wound was then grafted. The patient was alive and well without recurrence on August 21, 1950.

The pathological diagnosis was squamous cell carcinoma, grade 2.

CASE 8. W.O., an 81 year old white man, was admitted on August 1, 1947, complaining of an ulcer of the scalp. At the age of 1 year, he fell into a fire and received a severe burn of the scalp. It did not heal until he was 7 years old. When he was 16 years old, an ulcer appeared in the scar that healed after a few weeks of treatment. Two years before the present hospital admission the patient fell and injured the scar. The resultant laceration did not heal and for the year prior to admission enlarged slowly. Examination revealed the presence of an ulcer on the posterior scalp, 5 by 7 centimeters in size. Enlargement of the regional lymph nodes was not described. The ulcerated area was excised surgically and the

outer table of the calvarium was removed. The defect was covered by a skin graft. The patient died 3½ years after treatment of arteriosclerotic heart disease without evidence of recurrence of the carcinoma.

The pathological diagnosis was squamous cell carcinoma, grade 2.

CASE 9. J.R., a 44 year old white man, was admitted on May 2, 1949, complaining of an ulcer on the anterior aspect of the left leg. Twenty-four years prior to admission he received severe electrical burns to several areas of the body. The burned area on the left leg did not heal for 3½ years. For the next 10 years it ulcerated and healed intermittently. For the 10 years prior to hospital admission, an ulcer had been present in it continuously. Upon examination there was a large ulcer on the anterior aspect of the proximal third of the left leg. Roentgenograms of the tibia showed an osteomyelitis underlying the ulcerated lesion. A low thigh amputation was performed. The patient refused to permit surgical dissection of the inguinal lymph nodes, and metastatic carcinoma appeared in them on September 8, 1949. In April, 1950, a firm mass arose in the left supraclavicular fossa. A biopsy of it showed metastatic carcinoma. Metastatic disease also developed in the right supraclavicular fossa, the right occipital region, and the third posterior rib on the right. The patient died with carcinoma in September, 1950.

The pathological diagnosis was squamous cell carcinoma, grade 2.

CASE 10. L.W., an 18 year old negro, was admitted on April 22, 1950, complaining of an ulcer in the popliteal region. When he was 3 years old, the entire left leg from the ankle to the hip was burned in a fire. The wound was grafted at the time of the burn and remained healed until the patient was 12 years old. Several areas in it then became ulcerated. He had had two earlier admissions to this institution for excision of the ulcers and grafting, but none showed carcinoma. Six months prior to the admission in April, 1950, an ulcer appeared in the popliteal region. It had been treated with scarlet red ointment. Examination showed the presence of an ulcer in the left popliteal area that was 3 centimeters in diameter. There was no enlargement of the inguinal or femoral lymph nodes. The ulcer was excised and the defect was grafted. On June 16, 1950, a radical femoral, inguinal, and iliac lymph node dissection was performed. Metastatic disease was present in the iliac lymph nodes. The patient was well without recurrent disease on August 3, 1951.

The pathological diagnosis of the ulcer and of the lymph nodes was squamous cell carcinoma, grade 2.

CASE 11. E.M., a 60 year old white woman, was admitted on February 2, 1951, complaining of an ulcer on the left wrist. When she was 3 years of age she fell into an open fireplace burning the left hand, left wrist, right cheek and chin. She did not recall that grafts were done at that time nor the length of time before healing of the burns occurred. Over the course of years, marked flexion contractures developed in both wrists. Twenty years previously she was said to have had a carcinoma of the left side of the lower lip in a burned area that was treated successfully with radium. Six months before admission an ulcer appeared on the dorsal aspect of the left wrist that slowly enlarged. Examination revealed the presence of scars resulting from the burn on the chin and left side of the face. There were marked flexion contracture deformities of scars of both wrists. On the extensor surface of the left wrist there was an ulcerated, fungating mass, 5 by 7 centimeters in size. There was no enlargement of the epitrochlear or axillary lymph nodes. Amputation of the arm was urged, but the patient steadfastly refused any surgery, and, therefore, she was treated with x-ray irradiation. She was well 6 months after the conclusion of therapy.

The pathological diagnosis was squamous cell carcinoma, grade 2.

The 82 cases accepted from the literature were from the following sources: 28 from the series of Treves and Pack; 23 from Roffo and Gandolfo (12); 9 each from Cornil and associates and De Felice; 3 each from Johnson and Macomber and Trabue; and 1 each from Sollier and Radaody-Ralorosy, De Bell and Stevenson, Willis, Pickerill, and Halford and Gotshalk.

GENERAL CONSIDERATIONS

Sixty-eight of the 93 patients were males and 25 were females. Perhaps the preponderance of males is a reflection of the influence of environment on the acquisition of scars of such character that carcinoma can develop in them. With the exception of acute burn scar cancer and certain basal cell carcinomas, the complications have occurred in scars from severe penetrating burns, and Treves and Pack have stated, in effect, that female children are more prone to acquire and to succumb to burns of this nature than males because of the character of their clothing. If this is true, the theoretical possibility that fewer females subjected to burns of this degree live to develop cancer may be just as important in the sex distribution as environment. There were only 2 negro patients. Eighty-seven were white, and the race of 4 was not stated.

All cases designated in the reports as epidermoid carcinoma, carcinoma or squamous cell carcinoma are herein called epidermoid carcinoma and comprise a group of 80 cases. Pathological verification of the clinical diagnosis was not available in 7 of them. Two of

the 7 died with cancer; 1 was lost with residual disease; 1 was followed for 8 years without disease; 2 were followed for less than 1 year; and the result on the remaining 1 was unstated. The clinical impression was not verified pathologically in 4 of the 13 basal cell carcinomas. All were living and well for less than 5 years after treatment.

Anatomically there was a preponderance of the carcinomas on the extremities. Thirty-five involved the lower extremities; 21, the upper extremities; 20, the face and neck; 9, the trunk; and 8, the scalp. Such distribution is in marked contrast to that recorded by Elliott and Welton for spontaneous carcinoma of the skin, who, in a report of 1,742 treated patients, indicated that over 90 per cent of the lesions were located on structures of the head and neck.

It is of further interest that all of the basal cell carcinomas occurred on the face and neck and that with only 2 possible exceptions the contact with the heat of the burning agent was only momentary and the skin area burned was small. In general, these burns were caused by "splattering" of hot materials such as oil, metal chips, and molten metal. One might assume that clothing would protect most other areas of the body from trauma of this order, but presumably the hands would be just as exposed as the face, yet no basal cell carcinoma occurred on them. The exceptions mentioned were 1 case in which the historical data said only that the burn was from a hot stove, and a second for whom the cause of burn was not mentioned.

The sources of the heat causing the burn were of such a great variety that significant conclusions cannot be drawn with respect to an analysis of the importance of the agent causing the heat as a carcinogenic agent. However, there is little question that the epidermoid carcinomas arose in scars that were more extensive and deeper than the basal cell carcinomas. It is of interest that 5 of the 8 patients who had lesions on the scalp fell into an open fire or fireplace during infancy.

Healing of the wound and subsequent ulceration. Eleven patients, 4 with basal cell carcinoma and 7 with epidermoid carcinoma, had burn wounds that never healed, periods of ulceration for them varying between 4 months (17) and 61 years (9). The time interval required for the healing of the original wound varied in 19 other patients between 3 months and 10 years. There were 11 patients in whom the healed scar ulcerated intermittently for long periods of time before its final breakdown occurred. One of ours (Case 6) had such complications for 57 years before the diagnosis of carcinoma was made and 1 of Treves and Pack's for 49 years. Others varied between 2 and 6 years. A fourth type of ulcer complication in the scar consisted of a prolonged period of constant ulceration, before carcinoma developed, of a scar that previously had been healed. Nine such cases were recorded that varied between 10 and 25 years. It is these groups of cases that lead us to believe that ulceration, in itself, of a healed scar is not necessarily indicative of carcinoma.

Such ulcers are exposed theoretically to carcinogenic agents not only with respect to occupation and environment, but also to medications applied to the wounds. Unfortunately no conclusions can be drawn in this aspect of the study since practically no information was recorded about occupation, environment, or medication.

Although the follow-up data were poor, there is little question that the prognosis is grave. Only 5 patients with epidermoid carcinoma and 2 with basal cell carcinoma were reported living and well for 5 years.

Pathological features. The microscopic pathology in our 11 cases of epidermoid carcinoma was studied with particular reference to the character of the epithelium adjacent to the margin of the malignant tissue, the nature of the ulcerated area, the physical relationship of the remaining dermal glands to the carcinoma, and elastic fibers.

In most instances, it was noted that there was gradual thickening and piling up of the nonmalignant epithelium and elongation of rete pegs as it approached the neoplastic tissue. However, in all instances, the basement membrane was intact in this thickened epithelial layer, and no evidence was noted of a tendency toward gradual invasiveness. In general, such epithelium lay upon scar tissue that was devoid of glandular structures.

An outstanding feature was the abruptness with which hypertrophied epithelium changed to frank neoplastic tissue. The line of demarcation was always sharp and clear. It is illustrated in Figure 1 and again in Figure 2 where one can also see the thick epithelium with normal basement membrane adjacent to the carcinoma. Abnormal epithelium in all of our material was present in the bed of the ulcer. We have not found an example of a granulating surface in which carcinoma was totally absent in the ulcer but present on its margins. Sebaceous glands, sweat glands, and hair follicles were not present in or adjacent to carcinoma and actually were absent for some considerable distance lateral to the margin of the malignant ulcer as indicated in Figure 3. Examples of these structures lying in fibrous tissue beneath the carcinoma were not found.

An elastic fiber stain is illustrated in Figure 4. Although a section of 1 specimen showed a definite, thick layer of elastic fibers just beneath normal epithelium that had indistinct margins and that terminated abruptly at the margin of the malignant ulcer, this layer was absent in all others. The elastic fibers in them lay scattered indiscriminately in scar tissue and seemed to be just as prominent, if not more so, adjacent to and beneath carcinoma as adjacent to nonmalignant epithelium.

Also illustrated in Figure 4, as well as in Figure 5, are examples of structures that microscopically resemble calcified epithelial pearls. They were observed in 2 specimens. They seemed to be more numerous in scar tissue adjacent to carcinoma than in the frankly malignant element of the lesion, but did appear in the latter location. Some were calcified around the periphery with epithelioid cells forming the outer margins.

The origin of these bodies is uncertain. Presumably they are remnants of dermal epithelial structures (epidermis, hair follicles, sebaceous glands, or sweat glands) that became enmeshed in the healing wound. Carcinoma was not observed arising from them.

The influence of the age at burn on the length of the latent period. It is generally agreed that the character of neoplastic disease in infants and children is quite different from that seen in adults, at least partly because of the infrequency of carcinoma of the breast, uterus, ovaries, stomach, intestines, and prostate in the young. It has also been suggested that the characteristic malignant neoplasms of children originate from the influence of different conditions than those of adults, although it has not been possible to estimate adequately the effect of environmental carcinogenic agents in infants and children. Moreover, animal experiments have not distinctly clarified the reasons for this apparent discrepancy.

The prominent apparent feature of the analysis of this material was the marked difference in the length of the induction period (that latent period between the age at the time of burn and the age at the time the diagnosis of carcinoma was made) when the patient was burned in youth as compared to that of a patient burned in old age. This study was limited to the 80 patients with epidermoid carcinoma and the results are illustrated in Tables I and II and in Charts 1 and 2.

Table I indicates that when the mean age at the time of burn increases, the length of the mean latent period decreases. When age is analyzed with respect to latent periods of varying lengths, as indicated in Table II, it was noted that as the length of the mean latent period increases there is a decreasing mean age at burn. These data are expressed graphically in Charts 1 and 2. There was wide range in latent periods in each age group as indicated by the black dots in Chart 1. Yet the mean and median slopes are similar. A similar situation is illustrated in Chart 2, the companion chart for Table II, although the extremes of the age at burn in relation to the latent periods are not quite as great as the extremes of the latent periods in relation to the age at burn as illustrated in Chart 1 and its companion, Table I. The distribution of patients in age periods at the time of the diagnosis of carcinoma is illustrated in Chart 3.

DISCUSSION

The origin of carcinoma in the scars of thermal burns represents, in a certain sense, an experiment in carcinogenesis in the human subject, but in contrast to usual laboratory studies it is influenced by a host of uncontrol-

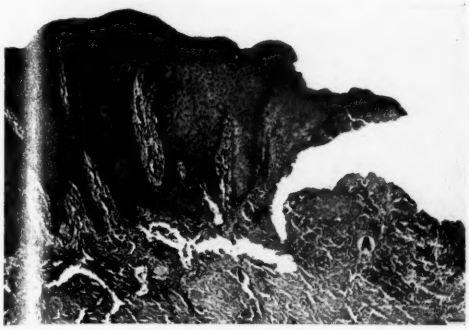

Fig. 1.

Fig. 2.

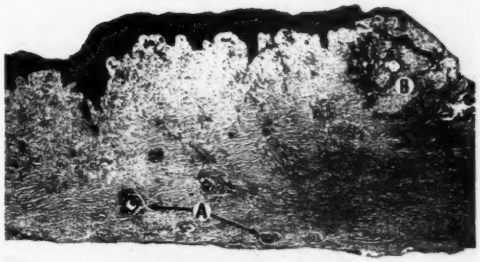

Fig. 4.

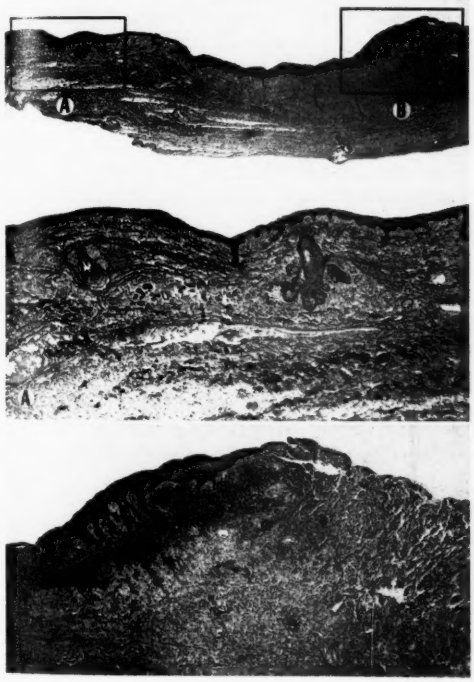

Fig. 3.

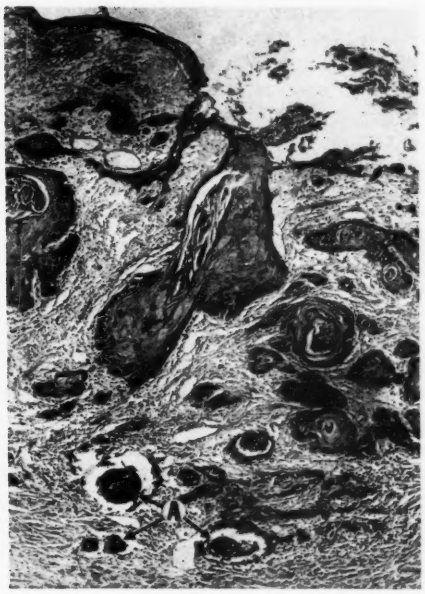

Fig. 5.

Fig. 1. The abrupt transition from thickened, but non-invasive, epithelium to cancer (*A*).

Fig. 2. Dense scar tissue underlying gradually thickening epithelium. Carcinoma present at *A*.

Fig. 3. A significant physical distance exists between normal sebaceous and sweat glands (*A*) and carcinoma (*B*).

Fig. 4. Elastic fiber stain. Calcified epithelial pearls at *A* (see text). Carcinoma at *B*.

Fig. 5. Structures resembling calcified epithelial pearls (*A*) in an area of carcinoma.

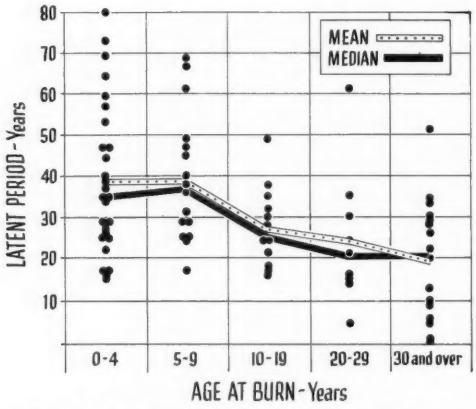

Chart 1. Relationship of age at time of burn to latent period.

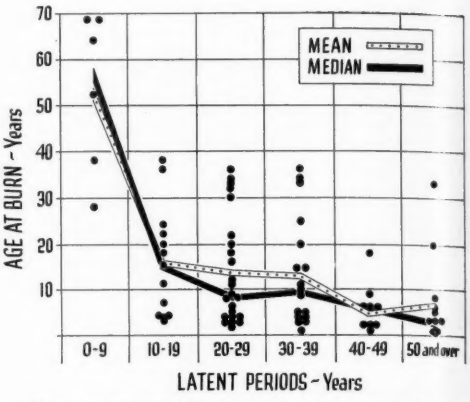

Chart. 2. Relationship of latent period to age at time of burn.

lable variables. The burning agent, severity of the burn, initial therapy of the wound as well as later therapy of recurrent ulcers, and occupation and environment of the patient in the years intervening before cancer are not subject to control. Even in retrospect, in following down such information, such wide discrepancies and particularly omissions are encountered that no valid conclusions can be drawn with respect to the importance of the broad field of environment in this type of neoplasm. Such omissions were just as common in our own records as in others and serve to re-emphasize the need for careful, accurate, and complete data in every study of environmental factors in human neoplasms. We are, therefore, unable to answer one of our original questions as to whether an ulcer in human patients that is known to have a margin of proliferating epithelium can be considered susceptible to environmental chemical carcinogens.

Again in contrast to usual laboratory procedures the two potential control groups of patients, one composed of those that develop carcinoma in unburned skin and the other of the burned patients who do not develop cancer in the burn scars, are themselves not controllable. A contrast that does exist, however, is the difference between the mean age at the time of the diagnosis of cancer in the above series, 47.2 years, and the mean age at the time of diagnosis of epidermoid cancer in the skin of unburned patients such as the ones reported from the Massachusetts and Huntington Hospitals which were 67.2 and 68.2, respectively (14). Even if our assumption that environmental carcinogens are effective in producing carcinoma in unburned human skin were correct, we still cannot determine the date at which such carcinogens first appeared in the environs. The mean age at the time of burn of the burned patients with epidermoid carcinoma in this study was 15.2 years, the mean latent period being 32 years. Probably the forces that are instigated by a burn that lead eventually to carcinoma in its scar are quite different from those that are effective on unburned skin; and we cannot assume that the induction period in these two groups would be similar.

We have no known way of studying the incidence and extent of burns of similar character that were grafted and never devel-

TABLE I.—AGE AT TIME OF BURN IN RELATION TO THE LATENT PERIOD IN EPIDERMOID CARCINOMA

Age in years at burn	No. of patients	Mean age at burn, yrs.	Mean latent period, yrs.
0–4	27	2.5	39.3
5–9	16	6.8	39.6
10–19	12	14.2	27.7
20–29	9	22.3	24.6
30 and over	16	41.7	19.8

oped cancer. However, the fact that only 2 patients in the above series with epidermoid carcinoma received skin grafts at, or shortly after, the time of burn is probably of considerable significance, and not only illuminates the prophylactic importance of this procedure, but also helps to clarify some thoughts on etiological factors that have previously been considered by others.

One would be led to believe that in the history of the management of burn wounds by grafts large numbers of patients with burns similar in extent and in method of origin to those herein described have been treated with early grafting. It is obvious that not many have developed cancer. If toxins released in burned tissue, or misplaced epithelial groups, or other substances really act as carcinogenic agents while embedded in human tissue, one would expect that they could also produce carcinoma in an overlying graft. On the other hand, one must admit that proliferating epithelium at the margin of an ulcer may be more sensitive to such carcinogens than that in grafted but healed skin.

Arguing from knowledge of known variations in host susceptibility, it is our opinion that many grafts would be susceptible. Since they apparently are not, we think it unlikely that carcinogens are embedded in the scar tissue. This opinion, together with our histological evidence that dermal appendage glands were not seen in association with the carcinoma which, furthermore, was not seen to arise from the "calcified epithelial pearls" makes us believe that the origin of the carcinoma is influenced solely by surface phenomena, whether from abnormal vascular supply, repeated trauma, carcinogens in environment, or a combination of these and other unknown situations, we cannot say.

TABLE II.—RELATIONSHIP OF LATENT PERIOD TO AGE AT BURN IN EPIDERMOID CARCINOMA

Latent period yrs.	No. of patients	Mean latent period, yrs.	Mean age at burn, yrs.
0–9	6	4.4	53.3
10–19	13	15.3	15.8
20–29	23	25.3	14.0
30–39	17	34.3	13.7
40–49	9	45.4	5.4
50 and over	12	63.8	7.0

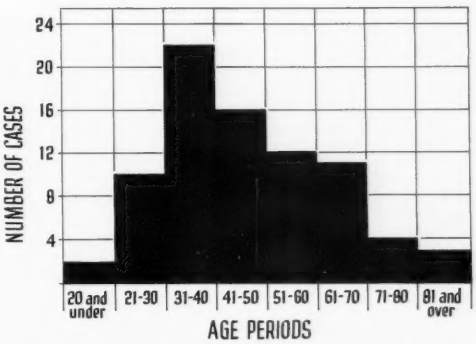

Chart 3. Distribution of patients in age periods at time of diagnosis of epidermoid carcinoma in burn scars.

Adequate conclusions cannot be drawn about the proper therapeutic management of the carcinoma complication. Although most of the reported patients have been treated by some sort of radiation therapy, it would seem that in view of the known poor vascular bed of these neoplasms, surgical removal of the lesion either by wide excision or amputation is therapy based on sounder logic than is radiation therapy. In this connection, the observations of Willis on a burn scar carcinoma patient should be mentioned. He described a patient who had had a burn scar carcinoma apparently completely excised, but who during the ensuing 15 months developed other malignant ulcers in the scarred area. He points out that such recurrences are not necessarily from incomplete removal of the tumor tissue, but may be from adjacent scar tissue undergoing malignant change, suggesting the need for wide removal of the predisposed field.

Evidence that infants and children develop different types of malignant neoplasms than adults is unmistakable and the assumption that this difference can be explained in whole or in part by the fact that adults have been subjected to different external influences cannot be questioned seriously. We are not aware of any other clinical study in which a similar cancerogenic stimulus (in this instance, the burn) has been applied to a group of patients of such a wide age range, 6 months to 69.6 years. Although Hueper has said, "it is obvi-

ous that burns sustained during childhood are apt to result in cancer at a considerably earlier age than thermic injuries suffered during adult life, possibly in the form of occupational accidents" (8), our statistical study does not verify this opinion. It shows a negative correlation between the age at burn and the interval to cancer, the coefficient of correlation being −.539.

We cannot explain the difference in susceptibility of the skin in the various age groups except to assume that a skin that is chronologically old has had an environmental experience that has made it more sensitive and prepared it to respond to the carcinogenic stimulus of a burn more quickly than a young skin. An excellent example of such preparation appears in the description of Treves and Pack's twenty-fourth case, where it is stated, the site of the neoplasm "had been the seat of chronic eczema following ivy poisoning. Keratotic warts had been cauterized by acids several times before the hand was burned."

SUMMARY

1. A series of 11 patients with carcinoma of the skin arising in the scars of thermal burns that have been treated at the Indiana University Medical Center were studied with 82 others reported in the literature for factors influencing the origin of such neoplasms.

2. No environmental hazards could be detected that appeared to influence the inception of the process.

3. Grafting of the wound at the time of burn is the best prophylactic measure.

4. The origin of the neoplasm seems to be a reflection of the effect of surface phenomena rather than of agents enveloped in the scar at the time of burn.

5. The length of the latent, or induction, period is inversely proportional to the age at burn.

REFERENCES

1. Bang, F. Le cancer des cicatrices; étude clinque et expérimental. Bull. Ass. fr. cancer, 1925, 14: 203–218.
2. Cornil, L., Paillas, J. E., and Bonneau, H. Le cancer des brûlures; à propos de 15 observations personnelles. Bull. Ass. fr. cancer, 1939, 28: 359–395.
3. Cramer, W. The origin of cancer in man. J. Am. M. Ass., 1942, 119: 309–316.
4. De Bell, P. J., and Stevenson, T. D. Squamous cell epithelioma of the extremities. Surg. Gyn. Obst., 1936, 63: 222–229.
5. De Felice, L. Il carcinoma su cicatrice da ustione nel suo significato biologico. Arch. "de Vecchi" per anat. pat. e med. clin., 1946, 8: 697–723.
6. Elliott, J. A., and Welton, D. D. Epithelioma; report on 1,742 treated patients. Arch. Dermat. Syph., Chic., 1946, 53: 307–332.
7. Halford, F. J., and Gotshalk, H. C. Epithelomatous degeneration in the scar of a burn. Arch. Dermat. Syph., Chic., 1941, 44: 26–29.
8. Hueper, W. C. Occupational Tumors and Allied Diseases. Springfield, Ill., and Baltimore, Md.: Charles C Thomas, 1942.
9. Johnson, F. M. The development of carcinoma in scar tissue following burns. Ann. Surg., 1926, 83: 165–169.
10. Macomber, W. B., and Trabue, J. C. Marjolin ulcer case reports. Plastic & Reconstr. Surg., 1951, 7: 152–156.
11. Pickerill, H. P. Malignant tumors following one application of an irritant. Lancet, Lond., 1926, 2: 854.
12. Roffo, A. H., and Gandolfo, A. Carcinoma desarrollado sobre cicatriz de quemadura; 25 casos observados en el Instituto do Medicinia Experimental. Prensa méd. argent., 1934, 21: 351–369.
13. Idem. Karzinombildung auf Brandnarben. Mschr. Krebsbekaempf., 1934, 2: 289–292.
14. Schrek, R., and Gates, O. Cutaneous carcinoma; a statistical analysis with respect to the duration and size of the tumors and the age of the patient at the onset and at biopsy of tumor. Arch. Path., Chic., 1941, 31: 411–421.
15. Simpson, W. L. An experimental study of single trauma malignancy. Cancer Res., 1947, 7: 726.
16. Sollier, N., and Radaody-Ralorosy, P. Evolution lente d'un épethélioma sur une cicatrice cutanée consécutive à une brûlure par la soude caustique. Arch. Soc. sc. méd. biol. Montpellier, 1938, 19: 431–436.
17. Treves, N., and Pack, G. T. The development of cancer in burn scars. Surg. Gyn. Obst., 1930, 51: 749–782.
18. Willis, R. A. Further studies on the mode of origin of carcinomas of the skin. Cancer Res., 1945, 5: 469–479.

OBSERVATIONS UPON THE ABSORPTION OF URINARY CONSTITUENTS AFTER URETEROSIGMOIDOSTOMY: THE IMPORTANCE OF RENAL DAMAGE

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WIDESPREAD interest in the absorption of urinary constituents from the colon after ureterosigmoidostomy has been expressed in the literature only during the last few years, although Bollman and Mann surmised in 1927 that the dog's colon could absorb urea after transplantation of the ureters into it. They found that the urea of the blood rose after the operation while the other nitrogenous constituents remained normal and no renal lesions could be found at autopsy. In 1931, from studies of a 10 year old boy with an old ureterosigmoidostomy, Boyd concluded that the presence of acid urine in the colon led to the excretion of fixed base by its mucosa, thus producing acidosis. Since his patient had hypocalcemia and rickets, he decided that calcium was lost after other basic ions had been depleted.

In 1940 Jewett had several dogs die after implantation of the ureters into the bowel without passing any urine, although their kidneys appeared normal. He cut the anal sphincter in subsequent experiments and the dogs survived. He later observed azotemia and acidosis in man after ureterosigmoidostomy, and concluded that both urea and chlorides could be absorbed through the mucosa of the colon.

Ferris and Odel, in 1950, noted hyperchloremia and acidosis in 79 per cent of 141 patients at varying intervals after their ureters had been transplanted into the colon. They found that the imbalance could be reduced or corrected by frequent evacuation of the bowel, by continuous irrigation of the colon through a two way catheter, or by unilateral nephrostomy. They therefore attributed the acidosis to the absorption of urinary chlorides through the bowel, and pointed out that the hyperchloremia and consequently the acidosis could be rectified by the administration of a low salt diet and sodium bicarbonate.

Boyce and Vest deduced that azotemia resulted from the absorption of urinary ammonia, probably as the chloride, from the bowel and its subsequent conversion in the liver to urea. They found that the instillation of ammonium chloride into the colon of the dog caused elevation of the urea and reduction of the carbon dioxide combining power of the blood. Boyce also produced hyperchloremia and acidosis by anastomosing the dog's colon to his bladder. After acidosis had appeared, he divided the colon above the anastomosis, closed the proximal end of the distal loop, and made a colostomy of the proximal loop. Since this corrected the hyperchloremic acidosis he concluded that the degree of absorption was related directly to the urea of colonic mucosa exposed to the urine.

Doroshow has suggested that a number of additional factors may upset electrolyte balance after ureterosigmoidostomy: organic acids excreted in the urine and others formed during fermentation may also be absorbed. Also, diarrhea may deplete supplies of water and base, while prolonged voluntary retention of the urine may promote its more complete absorption. Renal damage may interfere with the excretion of phosphates and with the formation of ammonia by the renal tubules, thus reducing the excretion of the chlorides. He observed some imbalance of electrolytes in 38.5 per cent of 52 patients without urographic evidence of renal injury after ureterosigmoidostomy.

Ferris and Odel, and Cordonnier and Lage have pointed out that hyperchloremic acidosis may be slow to appear after ureterosigmoid anastomosis, suggesting that renal disease is

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important in the development of the severer grades of imbalance, i.e., the latent period is due to the time required for the evolution of hydronephrosis and pyelonephritis. Since the latter investigators could not correlate the level of the nitrogen of the blood with the degree of hyperchloremic acidosis, and since Doroshow found the latter in the presence of grossly normal urograms, they assumed that tubular damage from infection may interfere with the excretion of chlorides before there is demonstrable retention of nitrogen or alteration in the urogram. The observation of Ferris and Odel that unilateral nephrostomy after ureterosigmoidostomy may correct hyperchloremic acidosis also supports this viewpoint. In other words, while the normal kidney can excrete the overload of chlorides imposed by their absorption from the bowel, the abnormal one cannot do so.

Lapides has made the most thorough study to date of the role of impaired renal function in the development of hyperchloremic acidosis following ureterosigmoidostomy. He stated that 59 per cent of 22 postoperative patients studied had hyperchloremia. Eighty-five per cent of these had acidosis, but the total base was normal in all of the latter. Most of those with hyperchloremia had had intermittent chills and fever. He observed that all patients and experimental animals coming to autopsy after implantation of the ureters into the colon had some degree of pyelonephritis, and that only 23 per cent of patients having urograms 6 months or more after such operations had normal appearing kidneys. Upon reviewing the literature he found that hyperchloremic acidosis may follow tubular damage from sulfonamides and nephrocalcinosis as well as from other factors. He also found that Raaschow had demonstrated by means of clearance tests that tubular injury is a prominent feature of pyelonephritis. Lapides, therefore, concluded that a patient with urographically normal kidneys could have enough tubular damage to produce hyperchloremia and acidosis.

He then demonstrated by clinical experimentation that renal impairment is of crucial importance in causing hyperchloremia after the absorption of urine or of some of its constituents from the bowel. In 3 patients whose renal function was normal, he collected the urine for 3 hours and allowed it to drip slowly into the rectum through a tube, meanwhile collecting more urine which was subsequently run into the bowel after expulsion of the first installment. This cycle was continued for 12 days in one patient and for shorter periods in the others. The addition of a contrast agent to the urine demonstrated that it reached the cecum, but no evidence of imbalance of electrolytes could be found during or after the experiments. The same experiment was then repeated in 3 patients with impaired renal function; all exhibited a rise of the nonprotein nitrogen along with hyperchloremia and acidosis.

Hypopotassemia after ureterointestinal anastomosis has been reported by Diefenbach, Fisk, and Gilson, by Foster, Drew, and Wiss, by Rosenberg and Elliott, and by Lapides. We have observed 2 cases and agree that it results, not from the presence of urine in the bowel per se, but from such nonspecific complications as anorexia, vomiting, and diarrhea (failure to ingest potassium while losing excessive amounts). It seems improbable that Korenberg's idea that all patients lose potassium after ureterosigmoidostomy can be correct, since hypopotassemia is an uncommon sequel of this operation. He apparently believes that sodium absorbed from the urine via the bowel replaces some of the cellular potassium, which is then necessarily excreted.

CLINICAL STUDY

The almost simultaneous admission to the hospital of 2 boys, who had had ureterosigmoidostomy in the first year of life yet presented entirely different clinical pictures, prompted this investigation. According to the literature there are four factors in the development of hyperchloremic acidosis: (1) the surface area of the colon exposed to the urine; (2) the frequency and completeness of evacuation of urine from the bowel; (3) the segment of the large intestine to which the urine is exposed; (4) functional capacity of the kidneys.

These studies have been carried out as opportunities have occurred, and so will not be presented in chronological order.

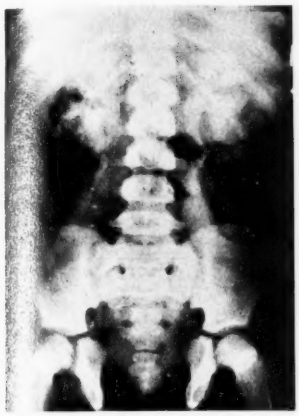

Fig. 1.

Fig. 2.

Fig. 3.

Fig. 1. D.B. Urogram taken on admission.
Fig. 2. D.B. Barium enema.
Fig. 3. D.B. Urogram taken after reimplantation of ureters.

CASE 1. D.B., University Hospital No. 736870, aged 7 years, had had a ureterosigmoidostomy in the first year of life followed by recurrent chills and fever. A transverse colostomy was therefore made 3 years later. The chills and fever ceased, but the patient was readmitted in October of 1950 because of failure to grow. The urea nitrogen of the blood was 44 milligrams per cent, the carbon dioxide combining power was 9, and the chlorides were 113 milliequivalents per liter. The excretory urogram (Fig. 1) showed greatly dilated ureters and renal pelves with obvious stenosis at the entrances of the ureters into the colon. The distal loop of the colon was greatly dilated and redundant (Fig. 2). The hyperchloremic acidosis was corrected and the azotemia reduced by continuous irrigation of the colon, forced fluids, and by the administration of alkalis. The ureters were then reimplanted into the colon at a higher level by direct anastomosis in an attempt to relieve the obstruction of the kidneys, although it was realized that this was already far advanced. Drainage of the kidneys was much improved (Fig. 3) but the urea nitrogen and the electrolytes returned to their former levels as soon as the rectal tube was removed after operation.

The second boy was admitted at about this time.

CASE 2. M.M., University Hospital No. 776011, had had a ureterosigmoidostomy during the first year of his life and he, too, then had recurrent chills and fever as a result of which transverse colostomy was done 1 year later. He had remained well since. He was an alert, normal appearing boy of 4. Excretory urography (Fig. 4) revealed a small right hydronephrosis and a normal looking left kidney. The urea nitrogen was 20 milligrams per cent, and the carbon dioxide combining power and chlorides were 21 and 109 milliequivalents per liter, respectively, a very mild, subclinical acidosis. His colon distal to the colostomy was normal (Fig. 5).

Impressed by the fact that the child with the normal colon had no significant imbalance of electrolytes, while the one with the dilated, redundant bowel had a severe hyperchloremia and acidosis, and influenced by Boyce's evidence that in the dog, the degree of absorption depended upon the urea of mucosa exposed to the urine, D.B.'s colon was excised from a point just above the entrance of the left ureter up to the colostomy. As long as an inlying rectal tube was used after this operation, electrolyte balance remained normal, but the imbalance returned as soon as it was removed. A year later the hydronephrosis had diminished perceptibly and the ureteral stasis had disappeared (Fig. 6) but the urea nitrogen had risen to 57 milligrams per cent, and the plasma bicarbonate and chlorides were 6 and 131 milliequivalents per liter. In other words, a pronounced reduction of the area of mucosa exposed to the urine had no influence upon the severity of the imbalance of electrolytes, suggesting that it was the renal damage that made it so severe, although its repeated disappearance after continuous irrigation of the colon demonstrated that absorption of chlorides from the bowel was the underlying factor.

While all who have observed patients for any length of time following ureterosigmoidostomy realize that hydronephrosis and pyelo-

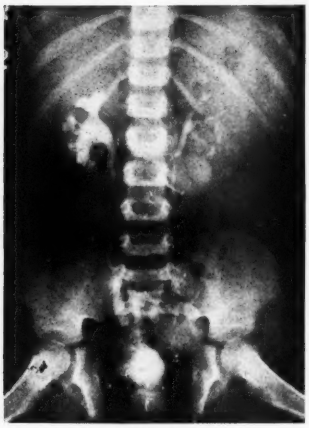

Fig. 4.

Fig. 5.

Fig. 6.

Fig. 4. M.M. Urogram made on admission.
Fig. 5. M.M. Barium enema.
Fig. 6. D.B. Urogram 1 year after reimplantation of ureters.

nephritis are frequent sequellae of this operation, there is in the literature relatively little information bearing upon this point. Harvard and Thompson reviewed 198 cases of exstrophy of the bladder treated by transplantation of the ureters into the colon, and were able to secure late urograms in 41 of them. Only 2 of these had normal appearing kidneys. Poole and Cook investigated 100 patients similarly treated for carcinoma of the bladder. Urograms were made 6 months or more after operation in 43; in only 5 did both kidneys look normal.

Lapides found normal urograms in only 5 of 22 patients 6 months or longer after operation. Thus in these three series of 106 cases, only 12 (11.3 per cent) had normal excretory pyelograms. Since only the more severe grades of pyelonephritis produce recognizable changes in the urograms, the actual incidence of renal injury is higher than was observed in these cases, and a longer period of follow up would show a still higher proportion of kidneys damaged.

Since the unphysiological operation of ureterosigmoidostomy exposes the normally sterile urinary tract to the infected contents of the colon, and since it is impossible to avoid with certainty some stenosis of the ureters and scarring of the colon at the site of anastomosis, a high incidence of renal disease is to be expected. Eighty-eight per cent of the cases just cited had evidence of renal lesions; 79 per cent of those investigated by Ferris and Odel had hyperchloremic acidosis. This suggests that there is a relationship between renal damage and hyperchloremia. Since the widespread adoption of direct anastomosis of the ureter to the colon without any attempt to minimize regurgitation of the contents of the colon into the ureter, it is not uncommon to see gas in the upper urinary tract after operation. Indeed, Whisenand and Moore have reported a case in which, following a "mucosa to mucosa" anastomosis in a patient with preliminary nephrostomies, gas and feces escaped from the tubes until they were removed, after which the tracts healed and the patient recovered.

In view of these unpleasant facts, it is surprising that more surgeons have not followed the suggestion made in 1895 by Mauclaire and in 1907 by Kroenig that a terminal colostomy be made above the anastomoses, thus providing a relatively clean reservoir for the urine.

Vest and Boyce have reported a case in which a preliminary colostomy was made and the distal loop irrigated with antibiotics prior to anastomosis; the urine was sterile 9 months after operation, which must be a world's record.

THE RELATIONSHIP OF RENAL DAMAGE TO HYPERCHLOREMIA AND ACIDOSIS

The records of 111 patients[1] who had had ureterosigmoidostomy were reviewed in an effort to make a rough correlation between renal injury and electrolyte imbalance. In 81 of these the urea nitrogen, plasma bicarbonate and chlorides had been determined between 6 weeks and 16 years after operation. The urea nitrogen was within normal limits in 41, and was elevated in 40.

Of the 41 with normal urea nitrogen, 23 or 65.6 per cent had normal values for the plasma bicarbonate and chlorides. The remaining 18 (44 per cent) had hyperchloremia, but only half of these had acidosis (22 per cent of the whole group with normal urea nitrogen), and only 1 (2.4 per cent) had symptoms.

Of those in whom the urea nitrogen was elevated, the incidence was quite different. Ten, or 25 per cent, had neither hyperchloremia nor acidosis, while 30, or 75 per cent, had hyperchloremia; 23 of these, or 70.6 per cent of the whole group with elevation of the urea nitrogen had acidosis, and 9 of these (22.2 per cent) had symptoms.

Comparing the two groups it is clear that renal damage sufficient to cause an elevation of the urea nitrogen is associated with hyperchloremic acidosis about 3 times as often as when the urea nitrogen is normal. This acidosis produces symptoms nearly 10 times as often when urea nitrogen is elevated.

Fifty-three of the 111 patients had both urograms and the chemistries under discussion done from 1 to 192 months after operation. Thirty of these had at least one normal appearing kidney; 7, or 23.3 per cent, had hyperchloremic acidosis; but only 1, or 3.3 per cent of the whole group, had symptoms.

Twenty-three of the 53 patients had unmistakable evidence of bilateral renal disease in the urograms. Thirteen, or 56.5 per cent, had hyperchloremic acidosis, and 9, or 39 per cent of the whole group of 23, had symptoms.

Therefore, hyperchloremia and acidosis were roughly 2½ times as common in the presence of gross bilateral renal disease, and produced symptoms more than 10 times as frequently as when one normal appearing kidney was present; the figures are almost identical with those concerning the urea nitrogen. These data seem to substantiate the impression that hyperchloremia and acidosis from the absorption of urinary chlorides from the colon after ureterosigmoidostomy *may* occur without gross renal disease but are found more often, are more severe, and produce symptoms very much more frequently if gross renal damage *is* present. It seems likely that, if more delicate tests of renal function were employed, a much higher incidence of renal disease would be found, and that this would account satisfactorily for the hyperchloremic acidosis found in those with normal levels of urea nitrogen in the blood and with normal appearing urograms.

It is not possible from our material to draw any conclusions concerning the absorption of urea nitrogen. Forty-one of the 81 patients, in whom the urea nitrogen was measured along with the carbon dioxide combining power and chlorides, had normal values for urea nitrogen. Among the 30 patients with normal urograms on at least one side, the urea nitrogen was elevated in 7, or 23.3 per cent, the highest value being 35 milligrams per cent. Among the 23 with urographic evidence of bilateral renal disease, the urea nitrogen was elevated in 18, or 78.3 per cent, almost an exact reversal. The highest value in this group was 118 milligrams per cent.

THE AREA OF COLONIC MUCOSA EXPOSED TO THE URINE

Case 1 demonstrates that reduction of the area of colonic mucosa exposed to the urine is probably not of critical importance, at least within reasonable limits, in determining the severity of hyperchloremia and acidosis when the kidneys are seriously diseased. In the third case, this aspect of the problem was studied a little further.

Case 3. L.F., University Hospital No. 750432, aged 38 years, had severe bilateral hydronephrosis secondary to a tightly contracted bladder filled with large papillomas. On admission the urea nitrogen was 38 milligrams per cent, the plasma bicarbonate was 19, and the chlorides were 102 milliequivalents per liter. Since he was neither dehydrated nor vom-

[1] 77 from the University Hospital, 25 from the files of our colleagues Drs. E. A. Webb and B. A. Smith, and 9 from the Minneapolis Veteran's Hospital.

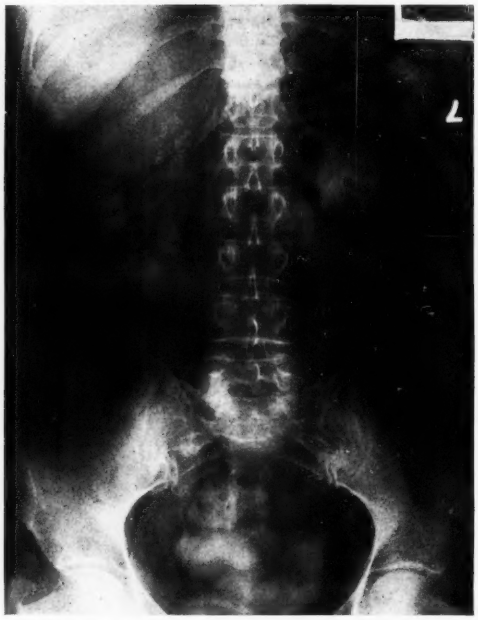

Fig. 7. A.G. Ascent of contrast agent to cecum 2 years after operation.

iting, the mild chemical acidosis was probably due to renal disease.

On October 3, 1950 ureterosigmoidostomy was done and, in order to protect his already badly injured kidneys as much as possible, the colon was divided between the descending and sigmoid segments. The distal end was closed and the proximal end was brought out as a terminal colostomy. It was discovered later that the capacity of the rectosigmoid was but 150 cubic centimeters, and that his control was poor, thus providing a minimal opportunity for the absorption of the constituents of the urine. Nevertheless, although the chemistries became normal while a rectal tube was left inlying during the immediate recovery, they returned to their former levels as soon as it was removed. By January 27, 1951, the urea nitrogen was 27, but the plasma bicarbonate and chlorides were 9 and 135 milliequivalents.

It seems unlikely, in the light of this evidence, that one can influence the severity of the imbalance of electrolytes satisfactorily by reducing the absorptive surface of the colon within practicable limits, i.e., if it is reduced enough to be effective, the urinary reservoir will be too small to be convenient for the patient.

The ineffectiveness of attempts to reduce the absorption of chlorides by lessening the exposure of the bowel to urine is also illustrated by the fourth case.

CASE 4. J.C., University Hospital No. 840276, had a terminal transverse colostomy and ureterosigmoidostomy for inoperable cancer of the bladder on January 26, 1952. The preoperative urogram had shown a moderate bilateral hydronephrosis, but the chemistries were normal before operation and remained so as long as the rectal tube was left in place after operation. It was removed on the seventh postoperative day and, 6 weeks later, the urea nitrogen was 26 milligrams per cent, and the plasma bicarbonate and chlorides were 14 and 111 milliequivalents per liter respectively. An attempt to visualize the distal loop of the large intestine at this time showed that contrast agent injected into the rectum would not pass above the level of the junction of the descending colon with the sigmoid, apparently because of kinking at the site of the left ureteral anastomosis. While the hyperchloremia was mild, it served to suggest that a short loop is no insurance against hyperchloremia if the kidneys are in any way abnormal.

Goodwin and Hudson have stated, without any evidence to support their views, that implantation of the ureters into the rectum ininstead of into the sigmoid will prevent hyperchloremia and acidosis because urine will not then ascend the colon. They made this statement because 2 patients so treated exhibited no evidence of hyperchloremia after a very short period of observation. Lapides has shown, however, that fluid introduced into the rectum can reach the cecum.

Our fifth case illustrates that, with good kidneys, urine may bathe the whole length of the colon for long periods without producing more than a mild hyperchloremia.

CASE 5. Mrs. A.G., University Hospital No. 817015, aged 65 years, had had ureterosigmoidostomy and cystectomy in March of 1950. In February of 1952 she felt perfectly well, having gained 30 pounds. She had observed no restriction of diet, and was in the habit of voiding once in 5 hours. The upper urinary tract appeared entirely normal in the urogram (Fig. 7); 90 minutes after injection contrast agent was seen in the region of the cecum. On February 7, 1952 the urea nitrogen was 25 milligrams per cent, the plasma bicarbonate was 24, and the plasma chlorides were 111 milliequivalents per liter. In other words, despite prolonged exposure of the whole length of the colon to the urine, her chlorides were only slightly elevated and there was no acidosis because the kidneys were efficient.

It seems safe to conclude from the data secured from Cases 3, 4, and 5 that the area of the colon exposed to the urine is of less importance than renal function in determining the severity of the electrolyte imbalance.

SEGMENT OF COLON EXPOSED TO URINE

Boyce and Vest have suggested that the *segment* of the colon which comes into contact with the urine is important in determining the amount of absorption of urinary constituents which will occur. They have concluded that the cecum of the dog has a greater capacity for absorption of electrolytes than has the rest of the colon. Merricks on the other hand maintains that the cecum of man has a smaller capacity for absorption than the rest of the large bowel. He bases this statement upon his experience with 12 patients whose ureters were anastomosed to the cecum. The ileum was then divided a short distance from the cecum, and its cecal end was brought out of the abdomen as an "artificial urethra," the ileocecal valve serving to prevent escape of urine in the intervals between catheterizations. The hepatic flexure of the colon was divided, the proximal end being closed and the distal end anastomosed to the proximal ileum. Thus the urine comes in contact only with the cecum and ascending colon. He has observed no evidence of hyperchloremic acidosis in any patient after this operation.

We have had no personal experience with this operation but, through the courtesy of Drs. Irving Victor, former resident in Urology at the Ancker Hospital in St. Paul, and William Mulvaney, his successor on the service of Dr. F. E. B. Foley, we have data on 1 case.

CASE 6. B.S., a male of 75, upon whom the operation just described was performed by Drs. Merricks and Gilchrist in Chicago in April of 1950. He was admitted to the Ancker Hospital in November of the same year for simple intestinal obstruction due to an adhesive band. He recovered after section of the band, and was then found to be in electrolyte balance. He remained so until June of 1951 when he began to have bouts of fever associated with leucocytosis. Shortly thereafter he was found to be in hyperchloremic acidosis. Excretory urography showed no evidence of excretion of the contrast agent, and attempts to catheterize the ureters through a cystoscope inserted through the cecum were futile. These attacks became more frequent and severe until they could no longer be controlled, and he died in January of 1952. Autopsy disclosed moderate bilateral hydronephrosis with severe pyelonephritis, the renal substance being largely destroyed (Fig. 8).

Fig. 8. B.S. Kidneys, ureters, and cecum secured at autopsy and injected with contrast agent before roentgenography. Note small amount of renal substance, especially on right. (Courtesy of Dr. William Mulvaney.)

Were it not for the evidence of the importance of absorption in the production of hyperchloremic acidosis, it would be tempting to assume that his imbalance was due to renal tubular injury alone. As it is, it seems safe to assume that the proximal large intestine can absorb sufficient chloride to cause serious imbalance when the kidneys are diseased.

SUMMARY AND CONCLUSIONS

It has been shown that the absorption of urinary chlorides through the mucosa of the colon after ureterosigmoidostomy can cause hyperchloremia and acidosis, thus accounting for the fact that many patients do not feel well after such operations in the absence of any hitherto obvious cause.

Four factors have been regarded as promoting this absorption: the surface area of the mucosa of the colon exposed to the urine; prolonged retention of the urine in the colon between urinations; variations in the absorptive capacity of the various segments of the large intestine; functional ability of the kidneys.

Clinical experiments with 5 patients and study of data from a sixth patient have shown that rather extreme shortening of the loop of the colon exposed to the urine, frequent evacuation of the urine, prolonged retention of the urine, implantation of the ureters into the cecum, and ascent of the urine to the cecum are of less importance in producing or preventing hyperchloremic acidosis than is the functional capacity of the kidneys.

Since infection of the kidneys together with some degree of hydronephrosis is almost inevitable after ureterosigmoidostomy as usually performed, and since there is no practicable way of preventing the absorption of the urinary chlorides, the solution to the problem would appear to lie in the prevention of infection and obstruction of the kidneys. Since the antibiotics thus far available are ineffective when administered for long periods, the most practicable countermeasure at the present time appears to be the performance of a terminal colostomy above the anastomoses. When the condition for which the operation is being performed is not malignant, a preliminary colostomy followed by irrigations of the distal loop with antibiotics to prepare a clean field for the ureters seems to be desirable.

With all its obvious disadvantages, a colostomy is infinitely more desirable than the otherwise almost inevitable pyelonephritis.

There are many interesting aspects of the alterations in electrolyte balance resulting from ureterosigmoidostomy which invite investigation in the laboratory and in the clinic.

REFERENCES

1. Bollman, J. L., and Mann, F. C. Nitrogenous constituents of the blood following transplantation of the ureters into different levels of the bowel. Proc. Soc. Exp. Biol., N. Y., 1927, 24: 923.
2. Boyce, W. H. Absorption of certain constituents of urine from large bowel of dog. J. Urol., Balt., 1951, 65: 241.
3. Boyce, W. H., and Vest, S. A. Role of ammonia reabsorption in acid-base imbalance following ureterosigmoidostomy. J. Urol., Balt., 1952, 67: 169.
4. Boyd, J. D. Chronic acidosis secondary to ureteral transplantation. Am. J. Dis. Child., 1931, 42: 366–371.
5. Cordonnier, J. J., and Lage, W. L. Evaluation of ureterosigmoid anastomosis by mucosa to mucosa method. J. Urol., Balt., 1951, 66: 565.
6. Diefenbach, W. C. L., Fisk, S. C., and Gilson, S. B. Hypopotassemia following ureterosigmoidostomy. N. England J. M., 1951, 244: 326.
7. Doroshow, H. S. Electrolyte imbalance after ureterosigmoidostomy. J. Urol., Balt., 1951, 65: 851.
8. Ferris, D. O., and Odel, H. M. Electrolyte pattern of blood after ureterosigmoidostomy. J. Am M. Ass., 1950, 142: 634.
9. Foster, F. P., Drew, D. W., and Wiss, E. J. Hyperchloremic acidosis and potassium deficiency following total cystectomy and bilateral ureterosigmoidostomy. Lahey Clin. Bull., 1950, 6: 231.
10. Goodwin, W. E., and Hudson, P. B. Exstrophy of the bladder treated by rectal transplantation of the ureters. Surg. Gyn. Obst., 1951, 93: 691–704.
11. Harvard, R. M., and Thompson, G. J. Exstrophy of the bladder; late results of treatment by the Coffey-Mayo method of ureterointestinal anastomosis. J. Urol., Balt., 1951, 65: 223.
12. Hinman, F., Jr. Ureteral implantation. J. Urol., Balt., 1950, 64: 567.
13. Jewett, H. J. Ureterointestinal implantation. J. Urol., Balt., 1940, 44: 223.
14. Idem. Ureterointestinal implantation in two stages. J. Urol., Balt., 1944, 52: 536.
15. Korenberg, M. Electrolyte disorders from ureterosigmoidostomy. J. Urol., Balt., 1951, 66: 686–687.
16. Kröenig. Die Anlegung eines Anus praeternaturalis zur Vermeidung der Colipyelitis bei Einpflazung der Ureteren ins Rectum. Zbl. Gyn., 1907, 31: 559–561.
17. Lapides, J. Mechanism of electrolyte imbalance following ureterosigmoidostomy. Surg. Gyn. Obst., 1951, 93: 691.
18. Mauclaire. De quelques essais de chirurgie experimentale applicables au traitement; de l'exstrophie de la vessie; des abouchements anormoux du rectum; des anus contre nature complexes. Congrés français de chir., 1900, pp. 546–552. Cited by Papin 1925.
19. Merricks, J. W. Personal communication, 1951.
20. Merricks, J. W., Gilchrist, R. K., Hamlin, H., and Riegel, I. T. A substitute bladder and urethra. J. Urol., Balt., 1951, 65: 581.
21. Mulvaney, William. Personal communication, 1952.
22. Nesbit, R. M. Elliptical anastomosis in urological surgery. Ann. Surg., 1949, 130: 796.
23. Poole, T. L., and Cook, E. N. Urographic study of the upper urinary tract prior to and after cutaneous ureterostomy and ureterosigmoidostomy. J. Urol., Balt., 1950, 63: 228.
24. Raaschow, F. Studies of Chronic Pyelonephritis with Special Reference to Renal Function. Copenhagen: E. Munksgaard, 1948. Quoted by Lapides.
25. Rosenberg, M. L., and Elliott, J. S. Resorptive acidosis following ureterosigmoidostomy. Stanford M. Bull., 1951, 9: 13.
26. Vest, S. A., and Boyce, W. Vesicosigmoidostomy for exstrophy of the bladder. Tr. Am. Ass. Genitourin. Surgeons, 1951, 43: 133.
27. Victor, Irving. Personal communication, 1951.
28. Whisenand, J. M., and Moore, V. Hydrodynamics of the upper urinary tract after mucosal ureterosigmoidostomy. J. Urol., Balt., 1951, 65: 564.

A NEW TECHNIQUE IN PRIMARY TENDON REPAIR

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THERE are few procedures in clinical surgery which result in as many disappointments as are seen in primary tendon repair. This is particularly true when one is dealing with tendons which are severed within the flexor digital sheath. Surgeons have attempted various methods and techniques to solve the tendon problem; but they have found no procedure which has given completely encouraging results.

Recently more attention has been directed to this problem, and several age old principles have been re-emphasized as the basis of success in the usual tendon repair. Accurate diagnosis and early treatment, aseptic technique, gentle handling of the tissues, and thorough follow-up care are considered essential in successful tendon surgery.

In order to aid in applying the basic principles of tendon repair, most surgeons have attempted to use a suture which is both simple and atraumatic. Mason points out that the ideal tendon suture should have a firm anchorage in the tendon, produce a minimum of disruption, avoid burdening the tissues with a great amount of suture material, leave the opposed tendon ends free of suture material, and should not leave knots between the stumps. Bunnell states that foreign body or suture material should be reduced to a minimum, suture should not strangle tissue, and a core stitch is preferable to a surface stitch.

A tendon suture is herewith presented which seems to very nearly conform to the standards of the ideal. This suture as previously described (2) was devised by Dr. Med. Fritz Lengemann and technically perfected in this country.

DESCRIPTION

This barb wire tendon suture consists of a 12 inch strand of braided tantalum wire with a straight needle on the distal end and a curved needle on the proximal end (Fig. 1). At approximately 8 inches from the straight needle, there is a V shaped steel barb which is applied in such a way that the prongs point toward the straight needle.

The technique in the use of this suture is extremely simple. The straight needle is threaded through the center of the proximal tendon segment, until the barb is engaged, starting the suture approximately ½ inch from the divided end. The straight needle is then inserted through the midportion of the distal segment and brought out through the skin. Adequate tension is placed on the distal portion of the suture and the severed ends easily approximated. This tension is maintained by means of a button with matchstick or lead shot. The proximal portion of the tendon suture is then threaded through the skin by means of the curved needle and loosely applied over a button. The suture in place can readily be seen by roentgenography (Fig. 2). Following the healing of the severed tendon, the suture is freed from the distal button and removed by gently pulling on the proximal button.

VERSATILITY

The applicability of this suture to tendons of various sizes and shapes has been tested (Fig. 3). In 14 consecutive unselected cases, representing 21 severed tendons, the suture has been applied with ease to extensor tendons as well as flexor tendons within and without the flexor digital sheath.

TISSUE REACTION

The question of trauma both to the tendon and to the surrounding tissue is of utmost importance in any suture technique.

In this series 1 patient had a combined tendon and nerve severance at the wrist. Six months following primary repair, the wrist was re-explored because of a neuroma of the

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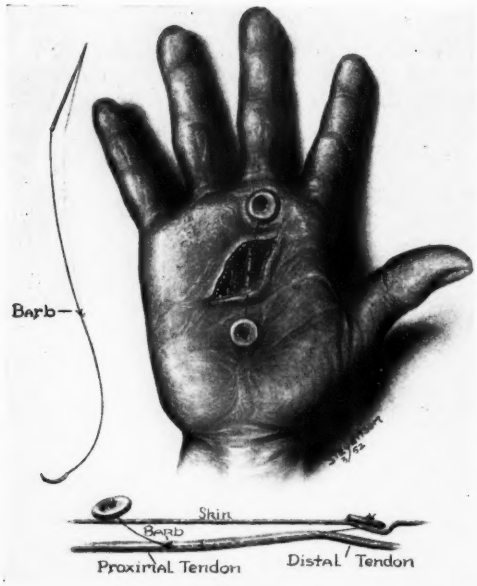


Fig. 1.

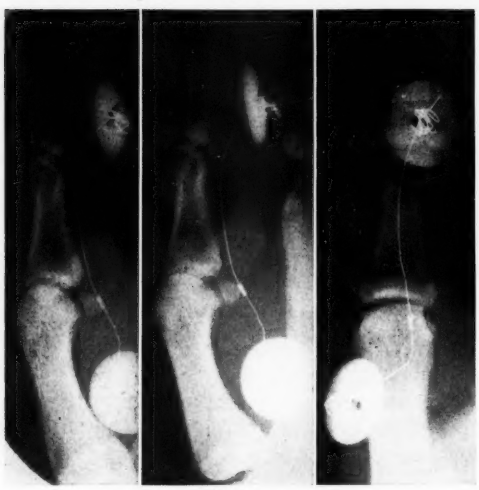


Fig. 2.

Fig. 1. Showing details of suture (left) drawing of hand with suture in place, and sagittal view (bottom).

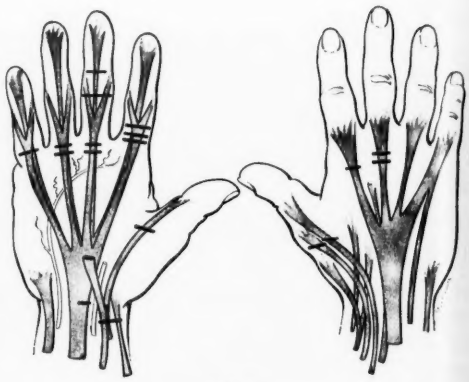


Fig. 3.

Fig. 4.

a b

Fig. 5.

Fig. 2. Roentgenogram showing suture in place.
Fig. 3. Diagram showing points of severance in first 21 tendons (14 cases). Flexor (left) and extensor (right) views.
Fig. 4. Exposed tendons showing black indurated areas from silk, sutures (bottom) and smooth glistening tendon sutured by special suture technique.
Fig. 5. Severance of extensor tendon, middle finger. a, Flexion; b, complete extension. No deformity.

median nerve. As some of the tendons had been sutured by standard silk technique and others had been sutured by the special pull-out suture, an evaluation of the relative amount of trauma could be made. The functional results of all the tendons was the same (Fig. 4). Yet, the tendons repaired by the barb wire suture remained shiny and smooth; those repaired by the silk technique showed evidence of induration and more tissue reaction.

a b

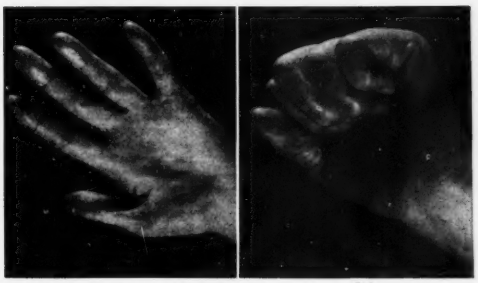
Fig. 6.

a b

Fig. 8.

a b

Fig. 7



a b

Fig. 9

Fig. 6. Severance of flexor pollicis longus at proximal phalanx. a, Extension. b, Flexion showing some flexor motion but restricted to 1 inch from head of fifth metacarpal. Fair result.

Fig. 7. Severance of both flexors to ring finger at metacarpal head. a, Extension. b, Flexion showing loss of approximately ¼ inch motion. Good result.

Fig. 8. Severance of both flexors of little finger at proximal phalanx. a, Extension. b, Flexion showing some profunda action but inability to touch distal palmar crease. Fair result.

Fig. 9. Severance of flexors to index finger, flexor pollicis longus, flexor carpi radialis, flexor carpi ulnaris, median and ulnar nerves. a, Extension showing some evidence of thenar wasting still present. b, Flexion showing complete return of function. Good result.

RESULTS

The results thus far obtained in the 21 severed tendons are evidence of the usefulness of this suture (Table I). However, this series is too small to attempt to evaluate any superiority over other techniques.

As would be expected by any technique, all 5 of the severed extensor tendons showed good end results. In one series reported by Miller 92 per cent of extensor tendon repairs healed without functional disability.

Similarly, of 5 flexor tendons severed at the wrist, all 5 gave good results. Of 11 tendons severed within the flexor digital sheath, 3 tendons were poor, 4 tendons were fair, and 4 tendons were good.

METHODS OF CLASSIFYING RESULTS

The criteria for good, fair, and poor results in this series are as follows: A result is considered good if the point of maximum function can be reached or approached to within a distance of 1 inch. In speaking of flexor

TABLE I.—SUMMARY OF RESULTS IN 14 CASES—REPRESENTING 21 TENDONS

Tendons	Good	Fair	Poor	Total
Extensors	5	0	0	5
Flexors (in sheath)	4	4	3	11
Flexors (not in sheath)	5	0	0	5
Total	14	4	3	21

tendons, the ideal would be for the tips of the fingers to reach the distal palmar crease, and for the tip of the thumb to touch the head of the fifth metacarpal. For the extensor tendons, the fingers should be perfectly straight (Fig. 5). A fair result is considered as one in which function is adequate for normal course movements of the hand; and one in which the point of maximum excursion is approached by more than 1 inch and by less than 2 inches. Illustrations of good and fair results are shown (Figs. 6, 7, 8, 9). Of the 3 poor results, 2 were linear lacerations in the proximal phalanges, resulting in contracture of the skin and inability to extend the fingers, even though the patient was able to use the fingers in flexion. The third poor result was complete failure with no flexor-profunda action following repair.

Because of the simplicity and ease of application of this suture, it is thought that it will prove to be a helpful adjunct in applying the basic principles of tendon repair. Further clinical investigation is being carried out to evaluate the merits of this technique.

SUMMARY

1. A new barb wire tendon suture is presented which seems to fulfill some basic principles in tendon suture technique.

2. Results obtained in 21 unselected severed tendons are presented.

3. Early impressions reveal an effective suture which may prove to be a useful adjunct in helping to solve the tendon problem.

REFERENCES

1. Bunnell, Sterling. Surgery of the Hand. 2nd ed., pp. 4–5. Philadelphia: J. B. Lippincott Co., 1948.
2. Mansberger, Arlie R., Jr., Jennings, Erwin R., Smith, Edward P., Jr., and Yeager, George H. A new type pull-out wire for tendon surgery; a preliminary report. Bull. Univ. Maryland School M., 1951, 36: 3.
3. Mason, Michael L. Primary and secondary tendon suture. Surg. Gyn. Obst., 1940, 70: 392.
4. Miller, Harry. Repair of severed tendons of the hand and wrist. Surg. Gyn. Obst., 1942, 75: 693.

THE TREATMENT OF IMPERFORATE ANUS AND ASSOCIATED FISTULAS

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THE management of imperforate anus has always presented major problems and the results of the classic forms of treatment have often been discouraging. Every surgeon dealing with this anomaly is familiar with the complications arising from the multiple, "staged" operations usually done for its correction. The mortality has been high and the morbidity, expressed in terms of hospital days resulting from these "staged" operations, is inestimable.

In recent years the one stage abdominoperineal procedure has been advanced as a solution to some of these difficulties. In 1948 we too adopted a more direct and radical approach to the problem, and we began a study of our cases in order to evaluate the treatment for the different forms of the anomaly. This report, with the accompanying illustrations by Dr. Lester Vargas, is based on our experience with 62 consecutive cases of malformations of the anus and rectum seen at the Columbia-Presbyterian Medical Center during the 3½ years between May 1948 and November 1951.

INCIDENCE

Most authors have estimated the incidence of anorectal anomalies to be about 1 in every 5,000 births, and some have placed it as high as 1 in every 1,500 births. The incidence is probably higher if one considers the cases of congenital anorectal stenosis which are not admitted to the hospital. This is suggested by Schapiro and by a recent report of Brown and Schoen, who found 39 congenital anorectal strictures while examining 100 consecutive infants brought to a well-baby clinic for routine care.

EMBRYOLOGY

It is not within the scope of the present paper to discuss embryology, and the reader is referred to the excellent descriptions of the development of this region found in Patten's textbook as well as in other publications (6, 13).

These malformations occur during the seventh and eighth weeks of fetal life. They are due to complete failure to rupture (imperforate anus) or to incomplete rupture (stenosis) of the anal membrane or failure of the urorectal membrane to separate completely the urinary and rectal anlages (urinary fistulas). In the female the muellerian ducts, which form the uterus and vagina, descend in the urorectal fold so that the fistulous connections usually occur in the vagina and not in the bladder or urethra as in the male.

The external sphincter muscle is derived from the regional mesoderm and is, therefore, not involved in these malformations. Clinically, although sphincter muscle fibers were seen in all of our dissections, there was a good deal of variation in the size and development of the muscle bundle in each.

TYPES OF MALFORMATIONS

There have been many classifications of these anorectal anomalies, but the method proposed by Ladd and Gross (7) in 1934 has been most generally followed since it is the most practical in determining therapy and prognosis. The four types are illustrated in Figure 1.

ASSOCIATED FISTULAS

From 55 to 82 per cent of the reported cases had an associated fistula and most of the connections were found in the type III anomaly.

In this group of 62 cases, in 44, or 71 per cent, a fistula was present. The forms of fistulas are illustrated in Figure 2 and their distribution is shown in Table I. It should be noted that all but 1 of the fistulas occurred in the type III anomaly.

Two forms of fistulas were seen in the *female*. The usual type was the rectovaginal

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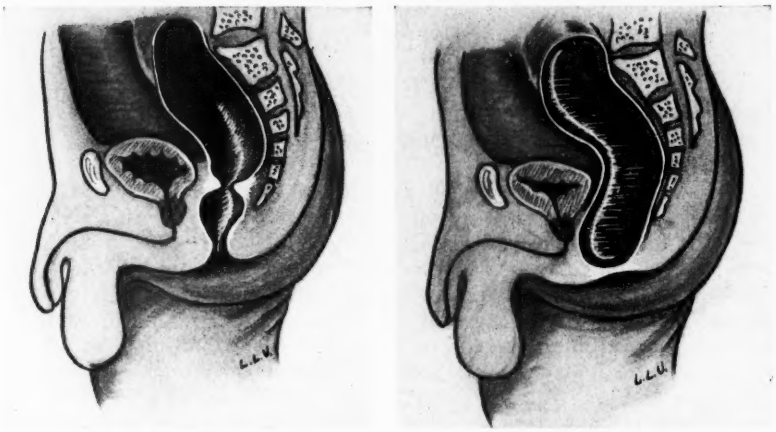
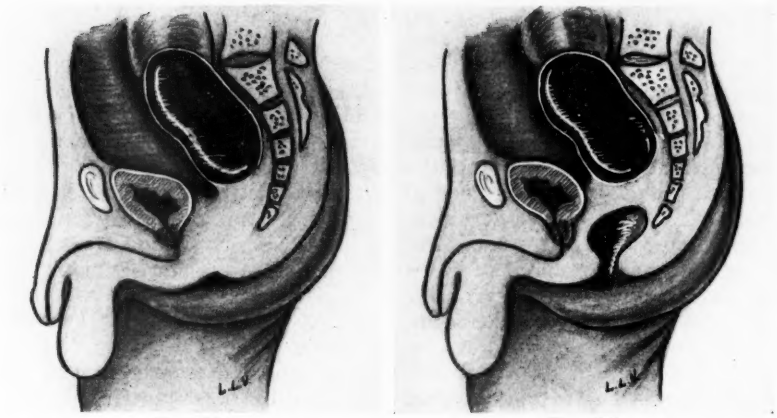


Type I Type II



Type III Type IV

Fig. 1. Types of malformations of the anus and rectum. Type I, Stenosis at the anus or lower rectum which is due to incomplete rupture of the anal membrane. Type II, Membranous form of imperforate anus. Due to a persistence of the anal membrane. Type III, The anus is imperforate and the rectum ends as a blind pouch a variable distance from the perineum. Type IV, The anal canal and lower rectum form a pouch which is separated, for a variable distance, from the blind rectal pouch.

in which the rectum entered the posterior vaginal wall just anterior to the fourchette in the fossa navicularis (Fig. 11). In 1 case the rectum presented high in the posterior vaginal wall. The other type was the rectoperineal in which the rectum opened on the perineum somewhere between the vaginal fourchette and the anal dimple. We have never seen a rectourinary fistula in the female.

In the *male*, two types of fistulas were seen: rectourinary and rectoperineal. There were only 2 cases with rectoperineal fistulas, i.e., the opening was between the perineoscrotal junction and the anal dimple. The usual fistula in the male was the rectourinary. The incidence of the specific types of rectourinary fistulas has varied in different series. Some authors have reported a predominant number of rectourethral fistulas in which the

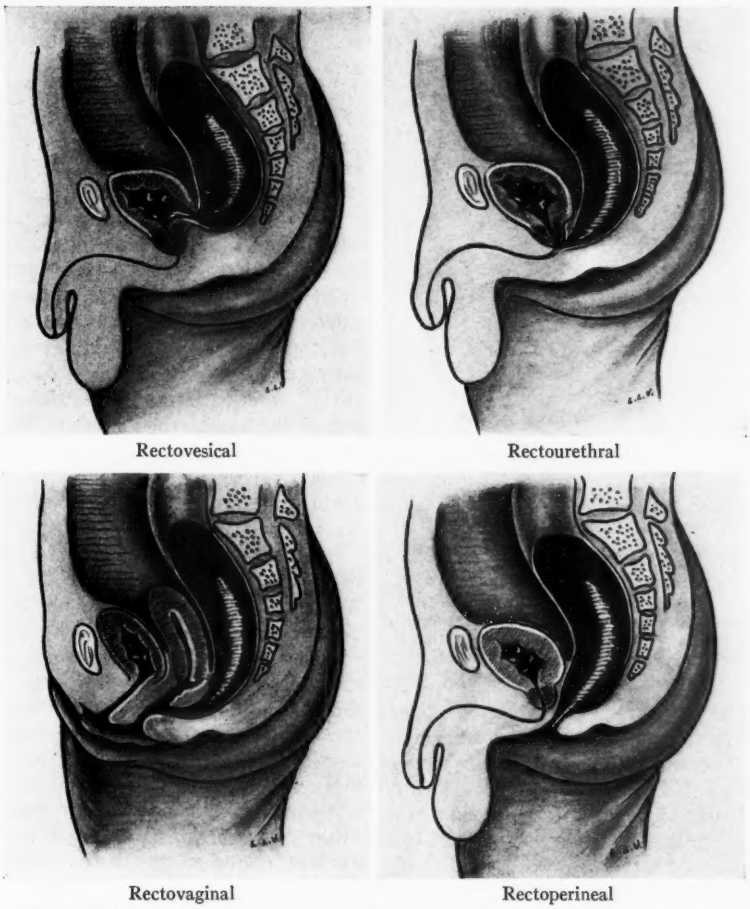


Fig. 2. Fistulas in type III imperforate anus: rectovesical, rectourethral, rectovaginal, rectoperineal.

connection was with the prostatic or membranous urethra. Others have found a greater proportion of the rectovesical type in which the communication was with the bladder at the trigone. We did not encounter any rectovesical fistulas in this series and in Figure 3 we have attempted to illustrate the type of rectourinary fistula which is representative of our cases.

CLINICAL DIAGNOSIS

Type I. This is an unusual form of the anomaly in most of the series reported as well as in ours. Only 4 of our 62 cases were of this type, 3 males and 1 female (Table I).

These patients may present symptoms soon after birth or not until months later, depending on the severity of the stenosis. Defecation is difficult and there may be ribbon-like stools. The abdomen becomes distended, fecal impaction may occur, and megacolon sometimes develops secondary to this chronic obstruction. The diagnosis is evident on digital examination.

Type II. This is also unusual. It occurred in 3 of our 62 cases, all males (Table I).

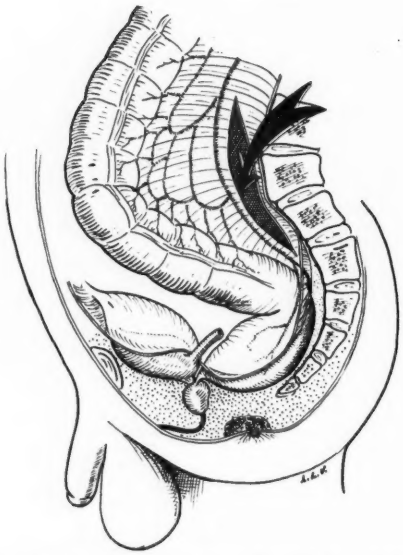


Fig. 3. Diagrammatic sagittal drawing of a type III anomaly in the male with the usual rectourethral fistula. Note point of entrance of the distal end of the rectum into prostatic urethra. (Arrow indicates plane of dissection to preserve superior hemorrhoidal vessels.)

The obstruction is apparent soon after birth as a very thin, bulging membrane which looks dark because of the meconium lying just behind it. No meconium is passed, and within 48 hours signs of intestinal obstruction develop unless there is an associated fistula, which may serve to empty the bowel, as occurred in 1 of our cases. Attention is called to the rarity of this type of anomaly. It is a very thin membranous obstruction which must be differentiated from the common type III anomaly for purposes of therapy.

TABLE I.—INCIDENCE OF TYPES, SEX, AND FISTULAS IN 62 CONSECUTIVE CASES

(May 1948 to November 1951)

Type	Male	Female	Total	Fistula in male	Fistula in female	Total fistulas
I	3	1	4	0	0	0
II	3	0	3	1	0	1
III	24	29	53	14	29	43
IV	1	1	2	0	0	0
Total No.	31	31	62	15*	29†	44
Per cent				48	93	71

*12 rectourethral (prostatic), 1 rectourinary—location unknown, 2 rectoperineal.

†20 rectovaginal, 9 rectoperineal.

Type III. This is the most common type of malformation accounting for 70 to 80 per cent of the previously reported cases. It occurred in 53 (85.5 per cent) of our 62 cases (Table I).

There usually is a depression (anal dimple) where one would expect to find the anus. In most cases this anal dimple is sharply defined; in others it may be less evident. The skin at this site is usually more deeply pigmented than the surrounding skin and the skin lines seem to converge to a central point within the external anal sphincter muscle which surrounds the dimple. Puckering can be seen at this central point when the anal sphincter contracts. When the baby cries or strains the area bulges forward, especially if the rectal pouch is low.

The external fistulas will be apparent in their location either in the posterior vaginal wall or in the perineum. The passage of air or meconium per urethra is evidence of a rectourinary fistula. A careful microscopic examination of the urine for meconium should always be done in the male who does not show gross evidence of a rectourinary connection. Some of the rectourinary fistulas or even the high rectovaginal fistulas may be temporarily plugged with inspissated meconium and their presence may not be clinically evident.

Signs of intestinal obstruction occur in those cases that do not have a fistula or whose fistula may be too small for adequate passage of stool. These patients are seen early, usually within 48 hours after birth. Those who have a fistula of adequate size may not seek medical attention until a later period when they are seen because of the anomalous opening or because of fecal impaction. In some cases there is a history of recurrent urinary infection.

Type IV. In this most unusual form of the anomaly (2 of 62 cases) the diagnosis may be delayed for a few days because of the normal appearing anus. However, no meconium is passed and signs of intestinal obstruction soon appear. The diagnosis is made on dig-

ital examination by palpation of the upper end of the anal pouch.

ROENTGEN DIAGNOSIS

Outlining the rectal pouch by roentgenograms taken with the baby in the upside-down position, as advocated by Wangensteen and Rice, may be helpful in determining the surgical approach. In the inverted position, the colonic gas rises to the rectal pouch and if a lead marker is placed on the anal dimple, one can estimate the distance between the end of the pouch and the skin, especially in the lateral views. The procedure is of little or no help in the type I anomaly and in other types that may have an adequate fistula, since the gas is expelled and does not outline the pouch.

Although we have used this method of examination routinely, we have found it of limited value, and at times misleading, since meconium at the distal end of the rectal pouch may prevent the gas from outlining the very end of the pouch, even in the inverted position, and one may gain an erroneous impression of the actual level of the blind rectum. Also, the speed of the distal progress of intestinal gas in the newborn varies so that the pouch may be outlined at the end of 4 hours in some cases, while it may take 24 hours or more in others. This period of delay may be of distinct technical disadvantage in the abdominoperineal approach because of the increasing distention of the sigmoid colon.

Roentgenograms may also be useful in a patient with a colostomy as a means of outlining the rectal pouch by introducing contrast medium into the distal colostomy loop. In some cases, a urinary fistula may be demonstrated by this method.

ASSOCIATED ANOMALIES

In 21 of the 62 cases (34 per cent) other developmental anomalies were present (Table II). Some patients showed more than 1 other abnormality. The incidence of associated malformations in other reported series varied from 28 to 46 per cent.

Many of the associated anomalies were of minor significance while some were serious.

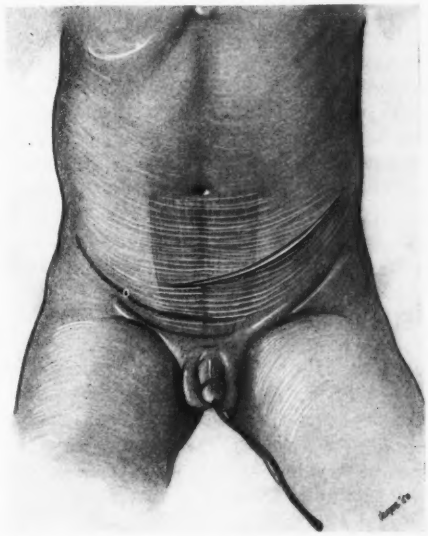


Fig. 4. Left lower oblique incision dividing entire left rectus and medial half of right rectus muscles. Urachus and lateral umbilical ligaments are to be divided well above the bladder.

Our 4 deaths were directly attributed to the coexisting anomalies, congenital heart disease in 2 cases and atresia of the esophagus with tracheoesophageal fistula in 2 cases. A

TABLE II.—ASSOCIATED ANOMALIES IN 62 CASES

Tracheoesophageal fistula	3
Duodenal stenosis	2
Congenital heart disease	2
Hypospadias, perineal	2
Bifid scrotum	2
Malformation of perineum, tumor?	1
Septate vagina	2
Anomaly of penis	1
Horseshoe kidney	1
Double ureter	1
Hydroureters	1
Clubfoot	3
Agenesis of arm	1
Absence of both radii	1
Absence of thumb	1
Hypoplasia of thumb	1
Malformation of index finger	1
Scoliosis	1
Hemivertebrae	1
Malformation of coccyx	1
Malformation of frontal bone	1
Congenital absence of rectus abdominis muscles	1
Mongolism	1

21 of the 62 cases (34 per cent) had one or more of these anomalies.

discussion of these deaths will be found in the section on mortality.

It seems worthy of mention that 3 patients in this group were successfully treated for other serious anomalies of the gastrointestinal tract in addition to imperforate anus. In one patient a congenital duodenal atresia was treated by gastroenterostomy, in another patient an esophageal atresia with a tracheoesophageal fistula was repaired, and in the third patient a congenital duodenal stenosis was treated by duodenojejunostomy.

TREATMENT

Type I. Gentle daily dilatations are carried out with a rectal tube or with graduated rubber dilators increasing the dilatations to the size of a No. 30 F catheter. If used properly, the small nasal speculum serves well and later the index finger may be used.

There were 4 cases in this group; 3 were treated by dilatation alone and 1 required incision of the stenosis followed by dilatations. Some cases reported in the literature (3) were treated by longitudinal incision of the stenosis followed by transverse suturing.

Type II. The treatment of the membranous form of imperforate anus consists of incision or excision of the anal membrane followed by dilatations.

There were 3 cases in this group. One of the patients had an adequate rectoperineal fistula which did not require immediate treatment. He died following repair of a tracheoesophageal fistula.

Type III. The treatment of this form of anomaly depends on the sex, the distance of the rectal pouch from the perineal skin, and the presence or absence of a urinary fistula.

TABLE III.—OPERATIVE PROCEDURES PERFORMED IN 60 PATIENTS

	No. procedures	Mortality
Dilatation or incision and dilatation	4	0
Transverse colostomy	5	1
Anoproctoplasty (males 4, females 25)	29	0
Abdominoperineal repair (males 21, females 3)	24	0
Abdominoanal anastomosis	1	0
Anoproctostomy	1	1
Total	64	2 (3.1 per cent)

In the male without a urinary fistula, the surgical approach is determined by the level of the rectal pouch as demonstrated by clinical signs and by the roentgenograms. If the blind end of the rectum is less than 2 centimeters from the anal pit, anoproctoplasty is performed by the perineal route.

A No. 8 or 10 F. catheter is passed into the urethra to act as a guide during the dissection. A vertical perineal incision is made starting in the anal dimple and carried posteriorly almost to the tip of the coccyx, dividing the posterior commissure of the external sphincter muscle. The rectal pouch is adequately mobilized from the surrounding structures so that it can be brought down to the level of the skin without tension. The pouch is opened and the meconium evacuated. The anus is then constructed by sewing the rectal wall to the skin with interrupted sutures of fine silk and the divided ends of the external sphincter muscle are approximated.

It has often been stated in the literature that if the rectal pouch is not "found" or if it cannot be adequately mobilized to be brought down to the skin without tension, a colostomy should be done. This assumes that the preoperative evaluation of the level of the rectal pouch was erroneous and that perineal "exploration" is advocated. Some of our cases were first seen after unsuccessful perineal exploration (often with packing of the perineal wound) followed by colostomy. The resulting cicatrix usually involving the external sphincter muscle, through which a perineal or an abdominoperineal operation had to be carried out, created some of our most difficult problems as regards anal function.

It should be emphasized that the perineal operation is not to be undertaken and that perineal "exploration" is contraindicated unless one is sure that the rectal pouch is low enough to be effectively mobilized and brought down to the skin. In our experience the rectal pouch should be no more than 2 centimeters from the anal skin if anoproctoplasty is to be accomplished without tension.

There were 4 cases of anoproctoplasty (Table III) performed for the type III anomaly in the male in this series. Two were in

newborns and 2 were in older children who were admitted because of anal stenosis with secondary megacolon following perineal operations at other hospitals.

In the male with a rectal pouch of over 2 centimeters from the anal dimple or with a urinary fistula, the combined abdominoperineal operation is the procedure of choice. It should be noted that the author is advocating this approach for all cases in which a urinary fistula is present no matter what the level of the rectal pouch.

This represents the most common anomaly in the male, and it is in this group that the classic form of treatment is usually unsatisfactory. The treatment often advocated consists of: A preliminary colostomy in the newborn period, division and closure of the urinary fistula accompanied by suprapubic cystostomy at the age of 4 to 9 years, repair of the imperforate anus at a later date and, finally, closure of the colostomy.

These multiple operations not only defer the final recovery of the patient but they may also give rise to a number of complications such as prolapse or stenosis of the colostomy and "distal loop trouble" of the colostomy, as recently described by Mayo and Rice. The patient, therefore, may find himself encumbered by the anomaly in some stage of treatment up to the age of 6 to 12 years or even longer and the morbidity, in terms of hospital days, must certainly be very high.

The combined abdominoperineal operation has simplified the problem by correcting the fistula and imperforate anus at the same time. The operative procedure is illustrated in Figures 4 through 10.

In the cases with a urinary fistula, the urethral catheter is left in the bladder for about 10 days postoperatively while the suture line in the prostatic urethra is healing. Its position is checked during the abdominal part of the operation, and it is sewed to the glans penis with a silk suture and later fastened with adhesive to insure its remaining in place. The patient usually voids normally after the catheter is removed.

Ether by the open-drop method was the anesthetic agent most commonly used. A few cases were done with cyclopropane. Routinely, before operation, a plastic catheter is placed in the internal saphenous vein at the ankle for the administration of blood and other fluids during and after operation. Small amounts of water are allowed orally as soon as the patient fully recovers from the anesthesia, milk is added by the second day and the diet is then increased as tolerated. Penicillin and streptomycin are used prophylactically and phthalylsulfacetimide is given orally for 5 to 7 days. The perineal sutures are removed on about the tenth day at which time gentle dilation of the anus is begun. Dilatation is repeated daily in the hospital and continued at home at increasing intervals. The patient is usually discharged from the hospital 3 to 5 weeks postoperatively.

The abdominoperineal operation was used in 21 males with a type III anomaly in this series without mortality (Table III). (It was also used in 3 females with a type III anomaly. This will be discussed later.)

In 7 newborns the one stage procedure was done without a colostomy. Ten patients, for whom a colostomy had been done in the newborn period before this study was begun, have undergone the abdominoperineal operation in this series. Most of these were under 7 months of age; the oldest was 5 years. All of the colostomies were closed 2 to 4 weeks after the abdominoperineal operation. In the remaining 4 cases in this group the procedure was done because of severe stricture of the anus and rectum which followed perineal operations performed elsewhere.

There were 2 operative complications: One patient who had a rectourethral fistula developed urinary retention after the catheter accidentally came out on the sixth postoperative day and required a suprapubic cystostomy. Urethral dilatations were necessary for a short period, and he is now voiding normally without evidence of urethral stricture 2 years after his last dilatation. The second patient developed a perianal abscess and later a fissure-in-ano which required excision.

In the female with a rectovaginal (Fig. 11) or rectoperineal fistula the usual type III anomaly was corrected by the perineal opera-

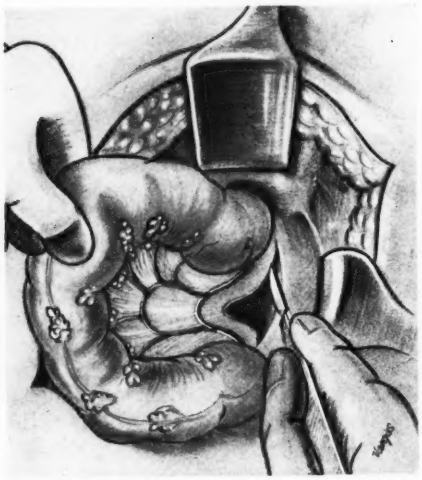


Fig. 5.

Fig. 7.

Fig. 6.

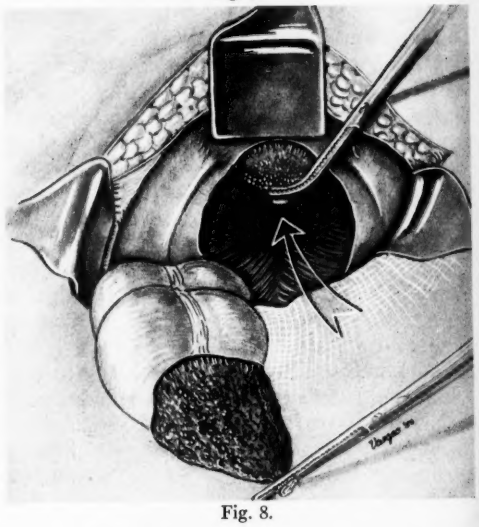


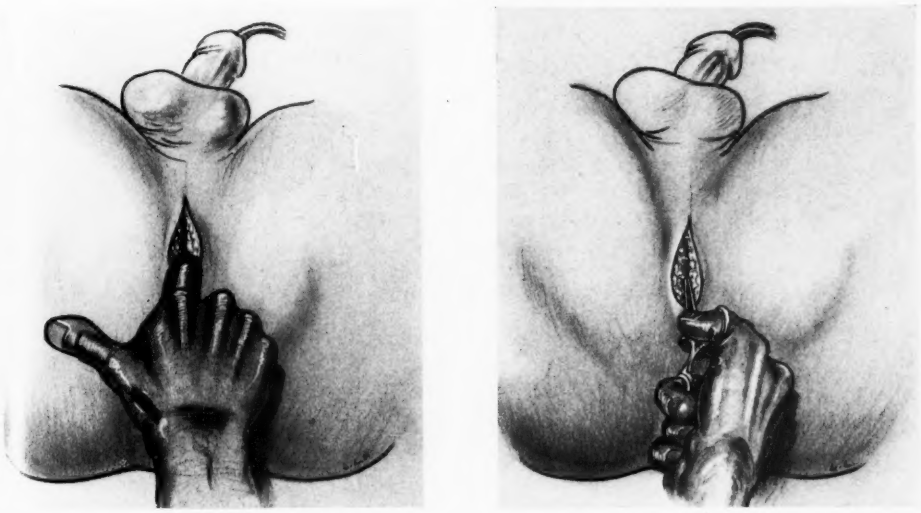
Fig. 8.

Fig. 5. Mobilization of sigmoid colon and rectum. Lateral and medial peritoneal attachments are incised and both ureters must be identified. The superior hemorrhoidal vessels are shown anterior to this dissection and are to be preserved. Gentle massaging of colon contents proximally will facilitate exposure.

Fig. 6. Further mobilization of rectum. Presacral space is entered behind the superior hemorrhoidal vessels which are shown on the bowel.

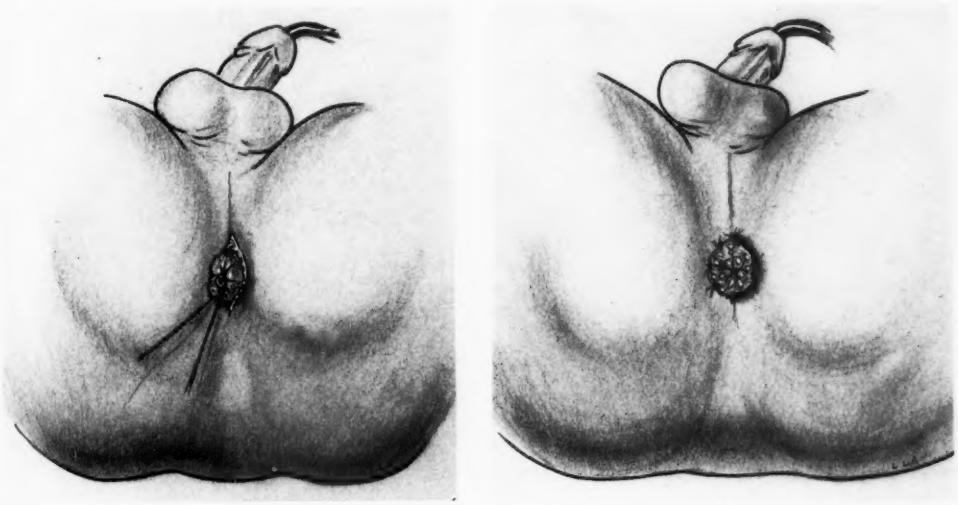
Fig. 7. Dissection has been carried down anteriorly below bladder. Rectum tapers and enters prostatic urethra. Note seminal vesicles. Palpation of indwelling urethral catheter aids in identifying urethra and point of entrance of rectum (the fistula).

Fig. 8. Division of rectourethral fistula leaving short stump at urethra, usually 3 to 4 millimeters. This distal end will be closed with fine chromic catgut. Clamp on proximal end of divided rectum to be replaced with ligature of heavy silk. (Arrow indicates point between levator ani muscles through which perineal wound will be joined.



a b

Fig. 9. a, Small vertical incision in anal dimple usually dividing posterior commissure of external sphincter. b, Insertion of long clamp into presacral space which will grasp suture on rectum.



a b

Fig. 10. a, Rectum brought through perineal incision. Enough rectum is brought down to preclude any tension on suture line. Abdominal wound is then closed. b, Anus is made by sewing rectal wall to skin with interrupted fine silk. Redundant rectum is excised as necessary. Ends of divided external sphincter approximated whenever possible.

tion. The bowel is prepared by oil retention enemas followed by saline colon lavages and phthalylsulfacetimide is given orally for about 7 days preoperatively. A special table, with leg holders and shoulder braces, is used for these perineal operations. The operative procedure is illustrated in Figures 11 through 16.

Streptomycin and penicillin are used pro-

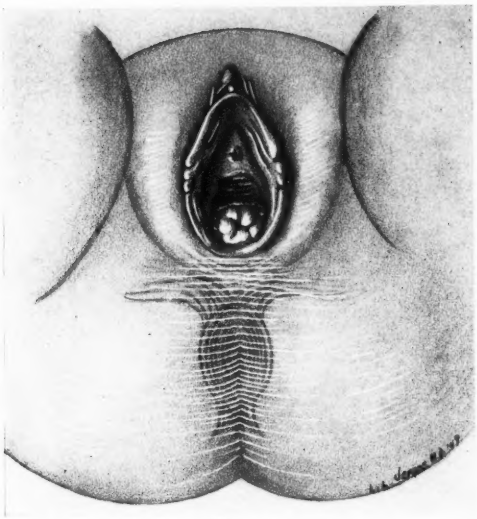


Fig. 11.

Fig. 12.

Fig. 13.

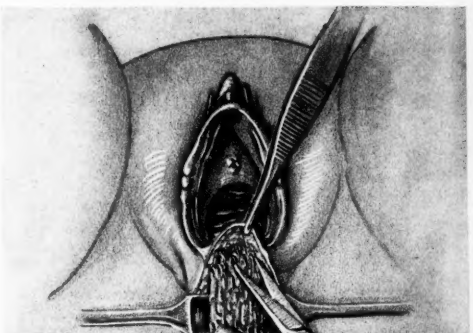


Fig. 14.

Fig. 11. The usual form of imperforate anus with recto-vaginal fistula. The rectal opening is seen in the posterior vaginal wall just above the fourchette.

Fig. 12. The incision encircles the fistula and is carried down into the anal dimple, dividing the anterior commissure of the external sphincter but preserving the posterior commissure. In some of the older patients it is not necessary to divide the sphincter as the rectum can be brought through a small incision within the intact muscle.

Fig. 13. The rectum is first mobilized posteriorly and laterally. Note the levator muscle fibers being separated from the rectum.

Fig. 14. Anterior dissection is performed. Note the rectum being separated from the posterior vaginal wall. The dissection must frequently be carried to the anterior peritoneal reflection in order that the rectum may be permitted to lay comfortably, without tension, in its new position.

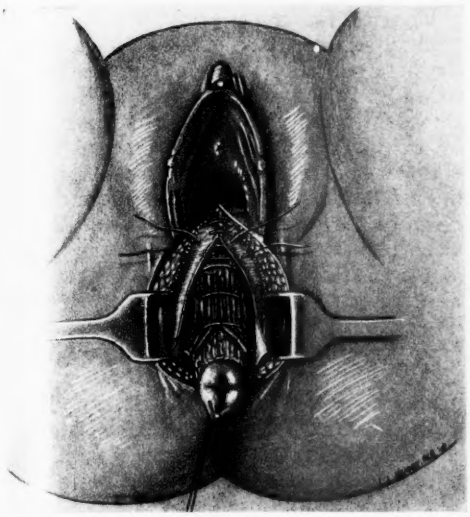


Fig. 15.

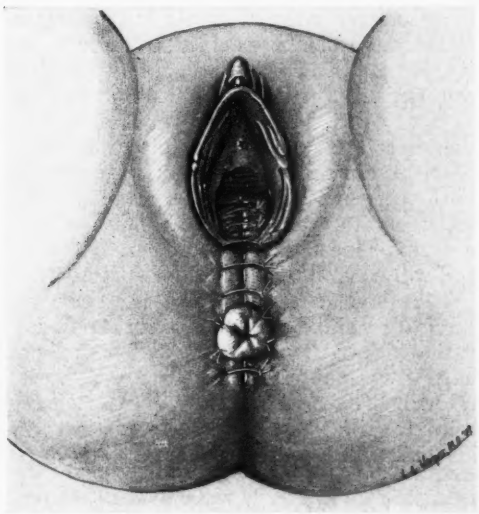


Fig. 16.

Fig. 15. Perineorrhaphy. Levator muscles and fascia approximated anterior to rectum with absorbable sutures.
Fig. 16. The divided anterior commissure of the external sphincter muscle has been reconstructed. Vaginal defect is closed with absorbable sutures. The fourchette and perineal skin are approximated with fine silk. Anus is made by sewing rectal wall to skin of anal dimple with fine silk. Redundant rectum is excised as necessary.

phylactically in the postoperative period, and phthalylsulfacetimide is resumed orally as soon as tolerated. Except for the very young patients, only clear fluids are allowed by mouth and opiates are used to keep the bowels from moving for about 5 days. These efforts are often unsuccessful, especially in the younger patients, and frequent cleansing of the sutures, under the direct supervision of the surgeon, is essential if one hopes to achieve primary union. After 5 days the diet is increased and mineral oil is started orally. The sutures are removed on the ninth or tenth day when gentle dilatations are started by the surgeon and then continued at home by the parents.

In this group of 29 females with the type III anomaly (Table I), in 25 the malformation was corrected by the perineal operation, in 3 correction was by the abdominoperineal procedure (Table III), and in 1 case operation has been deferred because of recent surgery for associated cyanotic heart disease.

A preliminary colostomy was used in only 2 of our 25 perineal corrective procedures. In the other 23 cases a colostomy was not used and it was gratifying to see all but 2 of them heal by primary union without any clinical infection. One patient, aged 6 years, developed fecal drainage from the perineal wound which required a sigmoid colostomy for diversion of the fecal stream. Secondary anoplasty was later done and she is awaiting closure of the colostomy as the perineal wound is healed. The other patient developed a mild infection in the perineal wound which caused some separation of the skin edges and undermining at the fourchette. This responded well to local treatment and the wound was sutured secondarily with good results.

The 3 cases requiring the abdominoperineal approach were unusual. One patient, who was 6 years old, was admitted with a sigmoid colostomy and a fistula high in the posterior vaginal wall. The second patient, aged 13 years, was admitted because of fecal impaction, severe megacolon, and a sigmoidovaginal fistula which followed several perineal operations for imperforate anus at another hospital. The third patient, who was 28 years old and recently married, presented

the usual rectovaginal fistula but had associated megacolon involving the rectum and sigmoid colon. The last 2 patients required resection of the hypertrophied rectum and sigmoid colon, in addition to correction of the imperforate anus and fistula. The megacolon seen in these 2 patients appeared to be of the congenital type. Imperforate anus associated with congenital megacolon has been observed in some of our more recent cases and will be reported in another article.

The time considered most favorable for surgical repair of this anomaly in the female varies with different authors. A few surgeons have advocated early operation, some have recommended that it be postponed until the third to fifth year, and others consider the ideal time for repair to be from 8 to 12 years. At the time of operation the age of our patients ranged from 6 days to 28 years. Eight were under 1 year, 6 were between 1 and 3 years, 13 were between 5 and 13 years, and 1 was 28 years old. We have adopted the policy of repairing the anomaly at any age for the following indications: (1) a fistula which is too small for adequate evacuation, (2) repeated episodes of fecal impaction (this can occur even with the large fistulas and may cause severe secondary megacolon in some cases), and (3) repeated ascending urinary infections. There have been 4 patients with the last complication. We do not recommend dilatation of a small fistula because of the cicatrix that follows, and would prefer to operate on these cases at an early age. In the patients with adequate fistulas who did not develop any complications, the repair was done as an elective procedure between the third and twelfth year.

Our immediate results lead us to continue this policy, as we have not yet reached any definite conclusion regarding the ideal age for the elective repair of this anomaly in the female nor have we been able to decide that there is any such optimum period. At this time, therefore, it would appear to the author that each case should receive specific evaluation and treatment on an individual basis.

Type IV. This most unusual form of the malformation was represented by 2 cases in this series, neither of which had a fistula.

The first was a 2 year old boy in whom a transverse colostomy had been done in the newborn period. Bowel continuity was established by an abdominoanal repair and anastomosis. The upper rectal pouch was freed, as in the abdominoperineal procedure, and a catheter was placed in the anus to help define the lower pouch, which was then mobilized down to the insertion of the levator ani muscles. The lower pouch was turned inside out and it was then opened on the perineum. The upper rectal pouch, was pulled through the lower pouch and an anastomosis was performed in the manner described by Swenson and Bill (15) and by Hiatt (5) in their treatment of congenital megacolon. The transverse colostomy was closed 3 weeks later.

The second case was a female recently admitted to the hospital at the age of 40 hours with congenital heart disease and an imperforate anus, which was at first mistaken for a type I anomaly with a complete membranous obstruction. Consequently, an opening was made into both pouches through the anus. Temporary decompression was thus achieved and on the fourth day the anomaly was actually visualized under anesthesia. The open rectal pouch was found to lie within the perforated anal pouch, and an anoproctostomy was easily done within the anus. Bowel function was good thereafter but the infant developed cardiac failure and died 4 weeks later.

OPERATIVE PROCEDURES

In 2 of the 62 cases in this series an operation was not performed for the rectal anomaly. A 5 year old girl has a type III malformation with an adequate rectoperineal fistula, but its correction has been deferred since she has just undergone a Blalock procedure for tetralogy of Fallot. The other patient was a 2 day old boy with a type II malformation and an adequate rectoperineal fistula who died 3 days following repair of a tracheoesophageal fistula.

The types of procedures performed in the 60 patients who were operated on are listed in Table III. It is noted that 64 procedures were carried out for correction of the anomaly in these 60 patients. Colostomies which were done preliminary to definitive treatment for

the imperforate anus account for the additional operations.

MORTALITY

Farin's immediate operative mortality recorded in 1931 was 32 per cent. In 1941 Ladd and Gross (8) had a mortality of 26 per cent with over a third of the deaths directly due to associated anomalies. Harken reported a surgical mortality rate of 20 per cent in 1942 and a 60 per cent overall mortality rate.

In recent years there has been a considerable decrease in the mortality rate following surgical correction of these anomalies. In 1943 Bacon and Hering reported a mortality of 11.2 per cent and more recently Norris, Murphy, and Brayton presented their group with an operative mortality of 9.1 per cent while Mayo and Rice recorded the identical figure in their series.

There were 2 deaths following operation in our cases, an operative mortality rate of 3.1 per cent (Table III). The first death occurred in a 2 day old boy with a type III anomaly and an atresia of the esophagus with a tracheoesophageal fistula who died 48 hours following repair of the esophageal anomaly and a transverse colostomy. The second death was in the girl with a type IV anomaly and congenital heart disease previously discussed who died in cardiac failure 4 weeks after anoproctostomy.

Four patients in the entire group died, a total case fatality rate of 6.4 per cent. One patient with a type III anomaly and many other associated malformations died suddenly at home from congenital heart disease, 3 months following a colostomy which was done on the first day of life. The second patient, a 2 day old boy with a type II anomaly and a large rectoperineal fistula which did not require operation, died 3 days following repair of a coexisting tracheoesophageal fistula. The third and fourth fatalities were considered to be operative and were discussed in the preceding paragraph. It should be noted that all the deaths in this series were due to associated anomalies.

RESULTS

In general, the results of treatment have been encouraging. The mortality was low, the morbidity has been greatly reduced, and operative complications have been rare.

Although it is apparent that the majority have, or can be expected to have, good anal function, complete assessment of this question is impossible at the present writing since many of our patients are in the early postoperative period or have not yet reached the normal bowel training age. For these reasons, many of the results are classified as "undetermined" and it will require careful follow-up study in the next few years to evaluate final results for the entire group. However, the following appraisal of our observations can be made:

All of the patients treated for the type I and type II anomalies now have excellent anal function.

The results for the 4 males who had a type III anomaly treated by anoproctoplasty were: 2 excellent and 2 good.

For the 21 males who had the abdominoperineal operation for a type III anomaly, the results were: 8 excellent, 5 good, 4 undetermined, 2 poor, 1 failure, and 1 unknown (not followed).

The 3 females who had the abdominoperineal procedure for a type III anomaly have good to excellent results.

The 25 females who had perineal repair of a type III anomaly have the following results: 10 excellent, 4 good, 9 undetermined, and 2 poor.

The 1 patient with the type IV anomaly who survived has an excellent result.

SUMMARY AND CONCLUSIONS

Experience with 62 consecutive cases of anorectal malformations over a 3½ year period is presented. Type III was the most common anomaly found, occurring in 85.5 per cent of the cases. Fistulas were seen in 71 per cent of the series, 93 per cent in the female and 48 per cent in the male.

The management of the different types of malformations was discussed. The practice of opening blindly into the rectum during the newborn period or of even "exploring" the perineum without preliminary study and evaluation should be discouraged.

The advantages of the combined abdominoperineal operation were discussed and the

technique described. The procedure was performed on 24 patients in this series without mortality.

The technique of the perineal operation in the female was presented. It would appear that preliminary colostomy was not necessary in the usual case.

The operative mortality rate was 3.1 per cent and the total case fatality rate was 6.4 per cent. All of the deaths were due to associated anomalies.

REFERENCES

1. Bacon, H. E., and Hering, A. C. The surgical management of congenital malformations of the anus, rectum and colon. J. Arkansas M. Soc., 1948, 45: 41.
2. Brown, S. S., and Schoen, A. H. Congenital anorectal stricture. J. Pediat., S. Louis, 1950, 36: 746.
3. David, V. C., and Gilchrist, R. K. Embryology and malformations of the rectum and anus. Nelson New Looseleaf Surgery. Vol. 5, p. 141. New York: Thomas Nelson & Sons, 1942.
4. Harken, D. E. Congenital malformations of the rectum and anus. Surgery, 1942, 11: 423.
5. Hiatt, R. B. The surgical treatment of congenital megacolon. Ann. Surg., 1951, 133: 321.
6. Keibel, F. and Mall, F. P. Manual of Human Embryology. Vol. 2, p. 306. Philadelphia: J. B. Lippincott, 1912.
7. Ladd, W. E., and Gross, R. E. Congenital malformations of the anus and rectum; report of 162 cases. Am. J. Surg., 1934, 23: 167.
8. Idem. Abdominal Surgery of Infancy and Childhood. P. 166. Philadelphia: W. B. Saunders Co., 1941.
9. Mayo, C. W., and Rice, R. G. Anorectal anomalies. Surgery, 1950, 27: 485.
10. Norris, W. J., Brophy, T. W., and Brayton, D. Imperforate anus; a case series and preliminary report on the one stage abdominoperineal operation. Surg. Gyn. Obst., 1949, 88: 623.
11. Parin, B. Atresia ani urethralis. Arch klin. Chir., 1931, 166: 386.
12. Patten, B. M. Textbook, Human Embryology. P. 569. Philadelphia: The Blakiston Co., 1947.
13. Pohlman, A. G. The development of the cloaca in human embryos. Am. J. Anat., 1911, 12: 1.
14. Schapiro, S. Discussion of author's paper at New York Proctological Society, April 13, 1950.
15. Swenson, O., and Bill, A. H. Resection of rectum and rectosigmoid with preservation of the sphincter for benign spastic lesions producing megacolon. Surgery, 1948, 24: 212.
16. Wangensteen, O. H., and Rice, C. O. Imperforate anus. Ann. Surg., 1930, 92: 77.

PECTUS EXCAVATUM

A Report of Eight Cases with Surgical Correction

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PECTUS excavatum, funnel chest, *trichterbrust*, and chonechondrosternon are all terms applied to a malformation of the anterior chest. The deformity so designated consists of a depression of the lower sternum and adjacent costal cartilages beginning at the manubriogladiolar junction and reaching its maximum depth at the xiphoid process. The deformity is usually congenital, being noted shortly after birth, and it may be progressive in degree until skeletal maturity is reached.

The actual incidence of pectus excavatum is uncertain since many mild cases go unnoticed. It has been reported as approximately 0.06 per cent. A hereditary influence in this condition is recognized. Sainsbury reported 6 cases of funnel chest among lineal descendants in a single family with no consanguineous marriage. His report strongly suggested that the deformity was inherited as a dominant character in this instance. He believed, however, that in the majority of cases it is probably transmitted as a recessive character and is not sex linked.

The etiology of pectus excavatum is not established. An overdevelopment of the "substernal ligament" has been suggested by Brown. Maldevelopment of the anterior muscular portion of the diaphragm from the embryonic septum transversum resulting in an unequal pull on the anterior chest wall is considered important by Brodkin. Partial obstruction of the upper respiratory tract (enlarged tonsils, laryngeal stridor) has been thought to be an etiologic factor. It seems probable to us that the deformity is a result of muscular-skeletal imbalance affecting the developing anterior chest wall, diaphragm, and related musculature, rather than a primary abnormality of bone. Rickets is not an etiologic factor.

Pectus excavatum is usually an asymptomatic lesion. Individuals with this deformity are typically of asthenic habitus, are sometimes poorly nourished, and usually display poor posture. They often show decreased resistance to infection, and chronic pulmonary disease such as bronchitis and bronchiectasis may be associated with advanced cases.

On the other hand a minority of patients have symptoms resulting from the deformity. These are cardiac, such as dyspnea, precordial pain, palpitation, and rarely decompensation, or pulmonary, including dyspnea, cyanosis, and cough. The reported cases of pectus excavatum with cardiorespiratory symptomatology have recently been reviewed by Ravitch.

Awareness of a funnel chest deformity, particularly in the female, may lead to abnormal shyness and withdrawal from social activity.

The diagnosis of pectus excavatum is quite simple and made by inspection alone. Paradoxical motion of the sternum may be seen in young patients. The electrocardiogram often shows a right-axis deviation. Measurements of the external diameters of the chest are essential in following the progression of the deformity, and this can be accomplished conveniently with the use of an obstetrical caliper.

Sporadic reports of operations designed to correct pectus excavatum appeared in the literature beginning in the early part of the century. These have been discussed in an exhaustive review of the subject by Ochsner and DeBakey. However, the operative treatment of this lesion was for the first time placed on a firm basis by Brown in 1939. Therapeutically he recognized two groups of cases. The

From the Department of Surgery of the Yale University School of Medicine, in contract with the Office of Naval Research, as part of Project N6ori-44, Task Order XI.

first comprised those under 2 years of age who may be improved by a limited operation consisting of division of the diaphragmatic and ligamentous attachments of the sternum. The second included older patients who require a more extensive procedure consisting of (1) freeing of the sternum through a midline incision, (2) resection of the depressed costal cartilages throughout the extent of the deformity, (3) transverse osteotomy at the manubriogladiolar junction with elevation of the depressed sternum, and (4) fixation of the sternum in the position of correction (with or without external traction).

The indications for operation are based on cosmetic, physiologic, and orthopedic considerations. The decision for operation depends on the extent of the deformity and evaluation of each case individually. The risk of an operative mortality should be negligible, but postoperative complications such as wound infection and mediastinitis, pulmonary infection, and pneumothorax have been observed. Since 1939 several series of surgically treated patients have been reported utilizing the operative principles suggested by Brown with good results.

The purpose of this paper is to report 8 cases of pectus excavatum which have been treated surgically. The first was operated on by the senior author while on duty in the U. S. Navy in 1945. The remaining 7 were treated at the New Haven Hospital from 1946 to 1951.

CASE REPORTS

CASE 1. J. C. This 20 year old white male was admitted to the U. S. Naval Hospital, Philadelphia, Pennsylvania, on August 27, 1945 with the complaint of chest pain. He gave a history of sternal depression since birth, and since the age of 10 he had been subject to attacks of sharp precordial chest pain which had become more severe in the past year. The attacks would last about 10 minutes and were not necessarily related to exertion. During the previous year he noted increasing dyspnea on exertion. He had a mild, nonproductive cough, present for several years, but denied hemoptysis, epistaxis, orthopnea, ankle swelling, or joint pains. He had lost 25 pounds in weight in the previous 5 months. Past history revealed scarlet fever at the age of 5 but no history of rheumatic fever.

Physical examination revealed an asthenic young man in no acute distress with a blood pressure of 110/80 millimeters of mercury. There was a marked sternal depression slightly to the left of the midline and maximal at the level of the xiphoid. The heart was displaced to the left and the heart sounds were normal. The lungs were clear, and there was no clubbing or edema of the extremities. Erythrocyte count was 4,320,000 with a hemoglobin of 13.0 grams per cent. The leucocyte count and urinalysis were normal, and the Kahn test was negative. Three sputum examinations revealed no acid-fast organisms. An electrocardiogram was normal. Roentgenograms of the chest revealed a marked sternal depression with displacement of the bulk of the heart into the left chest. There was approximately 4 centimeters distance between the depressed sternum and the dorsal vertebral column. The lung fields were clear. Vital capacity was reduced.

He was surveyed for discharge from the naval service, readmitted as a veteran, and on November 14, 1945 a plastic repair of the pectus excavatum was carried out through an inverted Y incision in the midline. The third through the seventh costal cartilages were resected through the extent of their deformity bilaterally, and the sternum was freed of posterior attachments. A transverse osteotomy through the manubriogladiolar junction was performed, and the sternum was elevated. A wire traction suture was placed through the sternum by means of drill holes, the wound was closed in layers and the ends of the wires were brought out through the lateral skin flaps and attached to a metal bridge. The bridge was fixed to the chest wall and the sternum elevated to a position of slight overcorrection. The postoperative course was uneventful, and the sternum maintained good position after removal of the traction sutures.

There were no further attacks of chest pain during his hospital stay.

In a communication from the patient on February 11, 1952 he states, "Since my discharge from the hospital I have had very little depression in the chest wall. The bone structure beneath the scar seems to be very strong and hard. I have had periodic examinations, and my heart, lungs, and blood pressure are normal. I have never had any pain or distress since the operation." He was recently married and is employed as a chemist.

CASE 2. L. A. Unit No. B86554. This infant male was first seen on June 29, 1946 at the age of 7 months. There was a history of sternal depression since birth which had steadily progressed. There had been episodes of difficult respirations and slight cyanosis. The infant had gained slowly and weighed only 15 pounds. No positive family history of pectus excavatum could be obtained. He was pale and underdeveloped. A pectus deformity was noted which had a 14 cubic centimeter capacity for fluid in the supine position, and the anteroposterior diameter of the chest at the xiphoid was 9 centimeters. The heart was enlarged to the left, and no murmur was audible. Other congenital defects were noted: external strabismus, bilateral clubfoot, corrected,

and undescended right testicle. Hemogram and urinalysis were normal, and an electrocardiogram was read as normal. Chest x-ray films showed a funnel chest deformity and a slightly enlarged heart.

On September 14, 1946 a limited operation consisting of xiphoidectomy and division of the substernal diaphragmatic and ligamentous attachments was performed according to the technique of Brown. The postoperative course was uneventful. Postoperative measurement of the chest revealed 9.5 centimeters in the anteroposterior diameter. During this admission a subtotal epiglottidectomy was performed by a consulting otolaryngologist, the diagnosis being congenital laryngeal stridor. Over a period of several months' follow-up the inspiratory stridor completely disappeared.

He was admitted again on June 8, 1947 for tonsillectomy and adenoidectomy and was followed in the ophthalmology and otolaryngology clinics through March, 1948.

He was seen again on October 13, 1950 at the age of 5 years. He had been active and apparently well without stridor; however, the pectus deformity remained. Lateral diameter of the chest was 16.5 centimeters, and anteroposterior diameter at the point of maximal depression was 9.5 centimeters. A machinery type murmur was audible over the pulmonic area. The other congenital defects were again noted. He was thought to have a congenital cardiac lesion, but extensive cardiac work-up, including cardiac catheterization, failed to demonstrate this. An electrocardiogram was again normal.

On March 6, 1951 a plastic repair of the pectus deformity was carried out through a midline incision. Costal cartilages three through seven were resected bilaterally through the extent of their deformity. A wedge sternotomy was carried out through the anterior cortex at the manubriogladiolar junction, and the sternum entirely freed of substernal attachments. The right pleural cavity was inadvertently entered. A wire suture was placed through drill holes in the anterior cortex of the distal sternum and brought out through the skin flaps. Following closure, the two ends of the wire suture were suspended from a metal bridge, resting on sponge rubber pads against the chest. The traction apparatus was removed on the thirteenth postoperative day without complication, and the repair appeared adequate.

Subsequently, the patient was admitted for orchidopexy on the right and resection of the levator tarsus on the left.

He was followed in the outpatient clinic and last seen on October 24, 1951 at which time the correction of the pectus deformity appeared good, and the patient was asymptomatic. Postural re-education was recommended for a slight dorsal kyphosis.

CASE 3. R. W. Unit No. C14303. This 9 year old white schoolboy was admitted June 7, 1948 with a history of a funnel chest deformity since infancy. He was the only child of an elderly primipara who was 39 years of age at the time of delivery. The pregnancy and delivery were considered uneventful and uncomplicated. His development was normal in all respects save for the chest deformity which gradually increased in extent. He had no unusual number of respiratory infections and engaged in strenuous athletics. An apical systolic murmur was first noted at the age of 18 months. Past history revealed chicken pox, mumps, and measles, the latter being complicated by an otitis which cleared in 2 weeks and caused no subsequent difficulty. No positive family history of funnel chest deformity could be obtained from the parents. Upon physical examination the vital signs were normal, and no clubbing of the fingers or kyphosis was present. The positive findings were limited to the chest which was symmetrical save for a sternal depression forming an oval deformity 6 centimeters in length and 7.5 centimeters in width. Paradoxical motion of the sternum was noted. The anteroposterior diameter of the chest at the xiphoid measured 12.5 centimeters on expiration and 11.5 centimeters on inspiration. The capacity of the deformity in the supine position was 14.0 cubic centimeters. A harsh apical systolic murmur was heard in the anterior axillary line. Chest films revealed only a sternal depression on lateral projection and slight displacement of the heart to the left on the anteroposterior film. A Mazzini test and a tuberculin skin test were negative. Blood count, urinalysis, and blood chemistries were within normal limits. An electrocardiogram was normal.

Surgical correction was accomplished under general endotracheal anesthesia through an inverted Y incision extending from the sternal angle to the xiphoid vertically with short lateral incision beginning at the inferior aspect of the vertical incision. Segments of the third through sixth costal cartilages were resected parasternally on both sides for a distance of 1.5 centimeters. The xiphoid was then mobilized and the substernal ligamentous attachments were transected. A transverse osteotomy was performed through the anterior cortex of the sternum at the manubriogladiolar junction. This permitted elevation of the depressed sternum which was maintained in a position of overcorrection by a silver wire passed through two drill holes through the gladiolus and fastened to an external metal frame attached to the anterior chest. The wound was then closed in layers. The postoperative course was uneventful and the silver wire traction suture was removed on the thirteenth postoperative day.

The patient was last seen on September 28, 1949 at which time the deformity was much improved, but not completely corrected. The anteroposterior diameter of the chest was 13 centimeters on expiration and 15 centimeters on inspiration. He was entirely asymptomatic. There was a keloid reaction at the upper portion of the midline scar.

CASE 4. A. P. Unit No. C28246. This 12 year old white schoolboy was admitted on July 5, 1949 with a history of funnel chest progressive since birth. He was entirely asymptomatic, being active

Fig. 1. Case 4 showing the deformity preoperatively. The depth of the depression was 5 centimeters below the anterior chest wall, and the anteroposterior diameter of the chest at this point was 12 centimeters.

in sports. There was no history of dyspnea, cyanosis, chest pain, palpitation, or cough. A heart murmur had been noted since early childhood and bilateral undescended testicles noted since birth.

The past and prenatal history was not remarkable. He was the third of four children, and there was no family history of pectus excavatum.

On physical examination he was well nourished but displayed poor posture of the kyphoscoliotic type. The upper respiratory tract was not remarkable except for slightly enlarged tonsils. There was no clubbing of the fingers. A depression of the lower sternum was present with an anteroposterior diameter of 12 centimeters at the maximum point of depression which was 5 centimeters below the anterior chest level (Fig. 1). Paradoxical movement of the sternum was noted on respiration. There was a loud systolic murmur heard over the entire precordium. The testicles were not felt in the scrotum, but could be palpated in the inguinal canals. Hemogram and urinalysis were normal, and a Mazzini test was negative. An electrocardiogram was considered normal, and chest x-ray films were not remarkable except for the depressed sternum and possibly slight rotation of the heart. Ventilatory function studies revealed a vital capacity of 2.6 liters and a maximal breathing capacity of 67.5 liters per minute.

On July 23, 1949 a plastic repair of the pectus excavatum was performed through an inverted Y incision in the midline. The third through the seventh costal cartilages were resected bilaterally through the extent of their deformity (from 2 to 6 cm. lengths), and the sternum was cleared of attachments posteriorly. An osteotomy of the anterior cortex was made at the manubriogladiolar junction, and the sternum was elevated. A double stainless steel wire was placed through the sternum by means of drill holes, the wound was closed in layers and the wires were brought out through the lateral skin flaps and attached to a metal bridge. The bridge was fixed to the chest wall and traction on the sternum was maintained with slight overcorrection. The postoperative course was benign except for a slight fever for a few days following operation. The bridge and the traction sutures were removed on the twelfth postoperative day (Fig. 2). A small collection (45 c.c.) of anterior mediastinal fluid was aspirated on the thirteenth postoperative day. This fluid was sterile on culture, and the patient was discharged 2 days later.

Follow-up visits revealed maintenance of good correction of the deformity and no paradoxical motion of the sternum on respiration. He was last seen on April 27, 1951, a right orchiectomy and left orchidopexy having been performed in the interval. The cardiac murmur was still audible, but less intense. There was keloid formation in the anterior chest scar and in both inguinal scars. He was gaining and growing well, and his posture was much improved.

Case 5. D. L. Unit No. C50542. This 11 year old white schoolboy was admitted on January 15, 1951 with the history of funnel chest since birth. Since the age of 5 years exertional dyspnea had been progressive until his activities were moderately limited. Shortness of breath occurred after climbing one flight of stairs. There had been no episodes of cardiac failure and no chest pain, angina, cyanosis, cough, or dysphagia. General development had been normal. He was subject to frequent upper respiratory infections and had pneumonia twice during childhood. There was no family history of pectus excavatum.

On physical examination he was rather small and thin and showed a moderated dorsal kyphosis. The upper respiratory tract was not remarkable. There was a sternal depression, maximal at the sternal xiphoid, and paradoxical movement of the sternum on respiration was apparent. The depression was 5 centimeters in diameter and 3 centimeters in depth. The anteroposterior diameter of the chest at the point of maximal depression was 10.5 centimeters. The lungs were clear, and a soft systolic murmur was audible at the cardiac base, the heart being otherwise normal to physical examination. There was no clubbing of the digits, and the remainder of the examination was not remarkable.

Hemogram and urinalysis were normal. Roentgenograms of the chest showed a marked sternal depression and slight displacement of the heart to the left. Emphysema of the left upper lobe was noted. The tuberculin test was negative. An electrocardiogram revealed RS-T and T wave changes

suggestive of an abnormal electrical axis of the heart. Cardiac catheterization studies revealed no intrinsic cardiac defect. Pulmonary function studies showed the vital capacity to be 1.53 liters and the maximal breathing capacity to be 58.3 liters per minute.

On January 25, 1951 a plastic repair of the pectus deformity was carried out under general endotracheal anesthesia through a midline incision from the manubrium to the midepigastrium. The third through the seventh costal cartilages were resected through the extent of their deformity bilaterally, and the xiphoid process was excised. The sternum was freed posteriorly, and a transverse osteotomy through the anterior cortex of the sternum at the manubriogladiolar junction was performed. A twisted stainless steel wire was placed through drill holes in the sternal body, and the two ends of the wire were brought out through the lateral skin flaps. The wound was closed in layers, and the traction wires were suspended from a metal bridge attached to the anterior chest wall, the sternum being elevated to a position of slight overcorrection.

The postoperative course was uneventful and the traction apparatus was removed on the thirteenth postoperative day. The correction was well maintained, postoperative electrocardiogram normal.

Follow-up 1 month later revealed a well healed and mobile chest without paradoxical movement. Pulmonary function tests at this time revealed a vital capacity of 1.14 liters and maximal breathing capacity of 73.3 liters per minute.

Bronchography, performed on March 30, 1951, revealed a normal bronchial tree, but showed at least 2 large emphysematous bullae in the left upper lobe.

He was last seen on July 20, 1951 and was asymptomatic with only slight exertional dyspnea. The cardiac murmur was not audible at this time. He has subsequently returned to school, and is to return to the clinic for further evaluation of the bullous emphysema of the left lung.

Case 6. C. M. Unit No. C58285. This 27 year old white single female school teacher was first seen on May 16, 1951 with the complaint of dyspnea on exertion. Since the age of 20 she had noted a gradual increase in exertional dyspnea and was unable to engage in strenuous sports, although walking and moderate activity did not cause shortness of breath. A funnel chest had been present since birth. She denied cyanosis, orthopnea, cough, chest pain or ankle swelling. Her past history was not remarkable, and there was no family history of funnel chest.

On physical examination she was a tall, slender, pale woman with a moderate dorsal kyphosis. The vital signs were normal. There was a pectus excavatum deformity, the maximum depression being at the sternal xiphoid. The anteroposterior measurements of the chest at the level of greatest depression were 15 centimeters on expiration and 17.5 centimeters on inspiration. The heart was normal to physical examination, and the remainder of the examination was not remarkable.

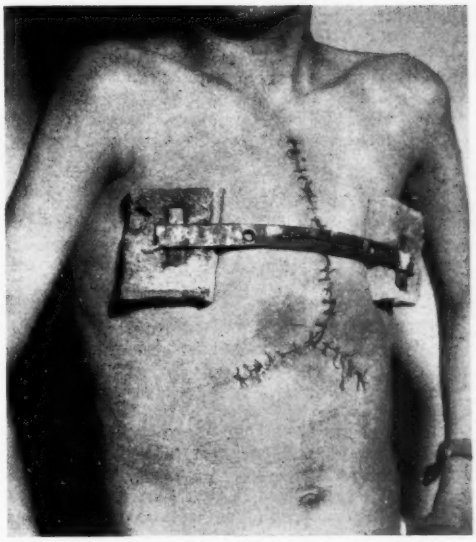

Fig. 2. The same patient showing the metal bridge and wire traction suture in place on the twelfth postoperative day just prior to removal. Note the overcorrection of the deformity by traction. The inverted Y incision has been replaced by a midline incision in subsequent cases.

Hemogram and urinalysis were normal. Chest roentgenograms revealed a depressed sternum and slight displacement of the heart to the left. On cardiac catheterization the right atrial pressure was elevated to a mean of 22 millimeters of mercury, and the cardiac output decreased to 3.42 liters per minute. Following digitalization the right atrial pressure dropped to a mean of 6.5 millimeters of mercury, and the cardiac output rose to a more normal level of 5.3 liters per minute. The vital capacity and maximal breathing capacity were 3.43 liters and 36.3 liters per minute before digitalization and 3.56 liters and 41.4 liters per minute after digitalization.

On July 19, 1951 a plastic repair of the pectus excavatum was carried out under general endotracheal anesthesia through a midline incision from the manubrium to the midepigastrium. The third through the seventh costal cartilages were resected bilaterally through the extent of their deformity, which in each case extended to the costochondral junction. The xiphoid was resected, and the sternum was freed posteriorly. In the course of dissection small openings were made in each pleural cavity. A transverse osteotomy of the anterior cortex of the sternum was performed at the manubriogladiolar junction. The sternum was elevated, and a double stainless steel wire was passed through the lateral wound flaps. The wound was closed in layers, and the left pleural cavity was aspirated with

a catheter. The traction wires were attached to a metal bridge which was fixed to the anterior chest wall, the sternum being elevated to a position of slight overcorrection. The patient ran a moderately febrile course for the first postoperative week, but this subsided. The traction apparatus was removed on the thirteenth postoperative day and she was discharged on the fifteenth postoperative day. Two days after discharge, she developed dyspnea, fever, and malaise. Physical and x-ray examination revealed a pleural effusion on the right which had not been present at the time of discharge. She was readmitted and treated with penicillin, streptomycin, and chloromycetin. Repeated thoracenteses were carried out during a 2 week period, and the fluid recovered consistently showed no bacterial growth on culture. She became afebrile on the seventh hospital day and remained so thereafter.

Follow-up examinations, the last of which was on November 21, 1951, revealed very little correction of the deformity but good stability of the chest. The lungs have been clear to physical and x-ray examination. The last anteroposterior measurements of the chest were 14.5 centimeters on expiration and 18.0 centimeters on inspiration. There was keloid formation in the central portion of the longitudinal scar. She is again teaching school, but has not yet attempted any strenuous activity.

CASE 7. D. L. Unit No. C63070. This 4 year old white boy was first seen on June 6, 1951 with a history of funnel chest deformity noted since birth and progressive since that time. Development had been otherwise normal. There was no history of dyspnea, cough, chest pain, or cyanosis. The child was not completely toilet trained at the age of 4. The past history was not remarkable, and there was no family history of pectus excavatum.

On physical examination the vital signs were normal. He appeared healthy but displayed a slight dorsal kyphosis. The upper respiratory tract was not remarkable. There was a pectus excavatum deformity with the maximum depression at the level of the xiphoid process. The anteroposterior measurement of the chest at the point of greatest depression was 8.5 centimeters, and the depth of the depression was 3.5 centimeters. The lungs were clear. The heart was slightly enlarged to the left, and the sounds were normal. There was no clubbing or cyanosis of the extremities, and the remainder of the examination was not remarkable.

Hemogram and urinalysis were normal. Roentgenograms of the chest revealed only the pectus deformity. An electrocardiogram was interpreted as normal.

On October 11, 1951 a plastic repair of the pectus excavatum was carried out under general endotracheal anesthesia through a midline incision from the jugular notch to the midepigastrium. The fourth through seventh costal cartilages were resected subperichondrially to the costal junction bilaterally. The xiphoid process was resected, and the sternum cleared of its posterior attachments. The sternum was elevated without the necessity of an osteotomy. A double stainless steel wire was passed through two drill holes in the sternal body, and its ends brought out through the lateral wound flaps. The wound was closed in layers, and the traction wires attached to a metal bridge which was fixed to the anterior chest wall.

The immediate postoperative course was uneventful. On the sixth postoperative day the traction suture was found to be broken, and the wire and bridge were removed. On the eighth postoperative day 60 cubic centimeters of fluid, which proved sterile to culture, were aspirated from the wound. There was a small separation of the wound edges at the inferior aspect which was healing well at the time of discharge on the fifteenth postoperative day. The lungs were clear, the correction of the deformity was good, and the patient felt well at discharge. He was last seen on February 13, 1952 at which time there was good fixation of the anterior chest. The anteroposterior diameter at the lower tip of the sternum was 10 centimeters on expiration and 14.5 centimeters on inspiration. A moderate dorsal kyphosis persisted for which postural education was recommended.

CASE 8. P. L. Unit No. C59733. This 6 year old white boy was admitted on July 22, 1951 because of a funnel chest deformity and a heart murmur. The deformity had been first noted at the age of 2 months and was progressive since then. There was a history of cyanosis on crying during infancy but not since. He was able to keep up with the other children at play, but seemed to become short of breath more easily. There was no history of cough, chest pain, palpitation, or ankle swelling. A heart murmur had been noted at the age of 3 months. There was no history of frequent or severe respiratory disease. The past history was not remarkable, and there was no family history of pectus excavatum.

On physical examination the vital signs were normal, and the child was small but well nourished and had a dorsal kyphosis. The upper respiratory tract was not remarkable. There was a pectus excavatum deformity with the maximum depression at the level of the xiphoid and slightly to the left of the midline. Paradoxical movement of the sternum with respiration was noted. The heart was enlarged to the left, and there was a systolic murmur heard best at the third and fourth left interspaces. The lungs were clear. There was no clubbing or cyanosis, and the remainder of the examination was not remarkable.

Hemogram and urinalysis were normal. Roentgenograms of the chest showed a pectus excavatum deformity and displacement of the heart to the left. An electrocardiogram was interpreted as normal. Cardiac catheterization studies were within normal limits. Ventilatory function studies revealed a vital capacity of 1.41 liters and a maximal breathing capacity of 43.3 liters per minute.

On July 26, 1951 a plastic repair of the pectus excavatum was carried out under general endotra-

cheal anesthesia through a midline incision from the sternal notch to the midepigastrium. The third through seventh costal cartilages were resected subperichondrially to their costal junctions bilaterally. The xiphoid process was resected, and the sternum freed from its posterior attachments. A transverse osteotomy through the anterior cortex of the sternal body was performed 1.5 centimeters below the sternal notch, and the sternum was elevated. A double stainless steel wire was placed through drill holes in the sternum and the ends brought out through the lateral skin flaps. The wound was closed in layers, and the wires suspended from a metal bridge fixed to the anterior chest wall.

The immediate postoperative course was somewhat stormy, and there was evidence of a small right pneumothorax. On the second postoperative day the traction wire was found broken, and consequently on the third postoperative day the wound was reexplored and a traction wire reinserted. The remainder of the postoperative course was uneventful and the traction wire was removed on the thirteenth postoperative day, the patient being discharged 2 days later. Roentgenograms of the chest showed correction of the deformity and no residual pneumothorax.

On September 14, 1951 the child was seen in follow-up and found to be asymptomatic with no cough, chest pain, or limitation of activity. The chest was well fixed, and there was good correction of the deformity with no paradoxical motion on respiration. The cardiac murmur was still audible.

DISCUSSION

All but 1 of these patients were males, and 6 of the 8 were operated upon before puberty. In none of the 8 cases was there a recognized family history of pectus excavatum. All had the onset of the deformity noted at or shortly after birth.

Only 1 patient, Case 1, had definite cardiac symptoms. Another (Case 6) had impaired cardiac function as evidenced by cardiac catheterization studies. Three others had cardiac catheterization with normal findings. However, 5 had cardiac murmurs (1 of which disappeared following operation) and 6 had roentgenographic evidence of cardiac displacement, all to the left. One had an abnormal electrocardiogram which became normal following operation. There was a variable decrease of pulmonary function in all of the patients. All showed some dorsal kyphosis. There was associated pulmonary disease in 1 patient (Case 5), namely, pulmonary emphysema. Two of the patients had other congenital defects, specifically, cryptorchidism (Case 5) and strabismus, clubfoot, and cryptorchidism (Case 2).

In all cases the more radical procedure for correction was performed, although a limited operation was done initially in one (Case 2) and did not prove successful in aborting the progress of the lesion. All of the patients were improved clinically with the exception of Case 6, in which follow-up has not been long enough for final evaluation.

There was no operative mortality in the series. Complications were few. In 2 cases the traction wires were found broken, one on the second and one on the sixth postoperative day. In neither case did this complicate the convalescence. A third (Case 6) was complicated by a pleural effusion postoperatively which responded readily to closed aspiration and chemotherapy. It is of interest that 3 of the 8 patients (Cases 3, 4, and 6) developed keloids in the surgical scar. This is far greater than the usual incidence of keloid formation in the white race and may be related to the position of the incision; however, in Case 4 keloids also developed in inguinal scars, suggesting a basic dyscrasia.

Certain technical considerations deserve emphasis. The supporting bridge is made of a malleable metal band which has been adapted to the patient's chest contour prior to operation. It is supported on the chest at the desired level on two sponge rubber pads. The pads are fixed to the skin with liquid adhesive in the anterior axillary line on either side. The pads, with the ends of the metal bridge, are then incorporated in the dressing at the conclusion of the operation. The sternum is elevated to a position of slight overcorrection to allow for any retraction after the wire is removed. Postoperative chemotherapy is essential since wound infection is a special hazard. Ambulation with the bridge in place is started on the first postoperative day, and efforts at postural education are begun at this time. In the case of a young child the physiotherapist visits the patient preoperatively to assure better co-operation during this early period.

It would appear that this operation is safe and should be recommended when indicated for orthopedic, physiologic, or cosmetic rea-

sons. Attention to postural habits postoperatively is essential. It is felt that the best cosmetic and functional results are obtained when the operation is done during early childhood, preferably between the ages of 4 and 8 years.

SUMMARY

The subject of pectus excavatum has been discussed. Eight cases treated surgically are reported. There were no operative deaths, and clinically the results were satisfactory in 7. Surgical treatment of pectus excavatum is best performed between the ages of 4 and 8 years.

REFERENCES

1. Brodkin, H. A. Congenital chondrosternal prominence (pigeon breast); a new interpretation. Pediatrics, 1949, 3: 286–295.
2. Brown, A. L. Pectus excavatum (funnel chest). J. Thorac. Surg., 1939, 9: 164–184.
3. Ochsner, A., and DeBakey, M. Chone-chondrosternon; report of a case and review of the literature. J. Thorac. Surg., 1939, 8: 469–511.
4. Ravitch, M. M. Pectus excavatum and heart failure. Surgery, 1951, 30: 178–194.
5. Sainsbury, H. S. K. Congenital funnel chest. Lancet, 1947, 253: 615–616.

SUBDURAL PURULENT COLLECTIONS

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IN reviewing our experience with intracranial abscesses of all types we have been impressed with the frequency of subdural abscess, and particularly the relative increase in incidence of this disease compared with brain abscess since the advent of the widespread use of penicillin. We will present the data from 16 cases of intracranial subdural purulent collections of varying etiology, review some major aspects of pathogenesis, comment on the surgical treatment, and discuss the postoperative management of the patients who survived. In each of the cases studied, free pus lay between the dura mater and the arachnoid. Other major intracranial purulent lesions were demonstrated in 7 cases.

The subdural space lying between the mesothelial inner lining of the dura mater and the outer (parietal) layer of the arachnoid has known significance as the site of collections of extravasated blood or of pus. Its size is of potential consequence only over the convexity of the cerebrum and to a lesser degree the cerebellum and the interhemispheric area. It is clinically insignificant at the base.

The tissues lining the subdural space participate in the encapsulation of extraneous material by proliferation and increased vascularization. This process is most marked on the dural side of the space (Figs. 1 and 2). The dura mater is particularly resistant to penetration by adjacent infection, but either wall of defense may be breached.

Subdural abscess can be classified from the etiologic standpoint, proved or theoretical, as follows:

1. Otitis media, acute or chronic, with or without mastoiditis, with or without cholesteatomatous formation.

2. Sinusitis: (a) acute or chronic, initiated or exacerbated by trauma (traumatic frontal sinusitis); (b) other accessory sinusitis: ethmoid, sphenoid, or maxillary.

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3. Trauma: (a) direct implantation such as by surgical manipulation during mastoidectomy or in the treatment of compound skull fractures; (b) following traumatic cellulitis of the scalp; (c) traumatic osteomyelits of the skull; (d) traumatic aerocele; (e) traumatic otitis media, mastoiditis, or frontal sinusitis; (f) rupture of a traumatic brain abscess.

4. Diffuse leptomeningitis.

5. Purulent rhinitis of infancy and early childhood.

6. Rupture of brain abscess.

7. Surgical drainage of brain abscess.

8. Metastasis, bacteremia, or septicemia.

9. Cavernous sinus thrombosis.

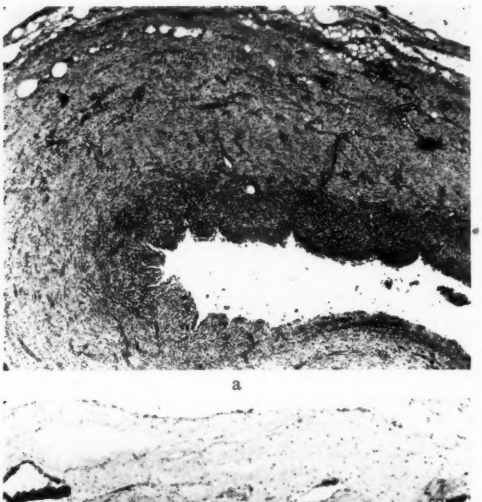
10. Miscellaneous: (a) scalp infection; (b) orbital abscess; (c) dental infection; (d) carcinoma of the face; (e) syphilis of the skull; (f) unknown.

The first four major groups warrant separate and detailed evaluation.

Subdural purulent collections secondary to otitis media. Prior to 1932 there were probably no more than 40 cases of otogenic subdural abscess in the literature. Subsequent analyses demonstrated the increasing incidence of recognition of the disease, and that about 40 per cent of all subdural abscesses were otogenic in origin. Whether the chronicity of the otitis media is significant in the pathogenesis is disputed. Our opinion is in accord with that which recognizes that acute as well as chronic forms of otitis media are responsible for the lesion.

There are 3 modes of formation of subdural pus from middle ear infection:

1. Extension by contiguity of the purulent process. This occurs through necrotic defects in and penetration of the dura mater with or without coexistent neighborhood reaction such as petrositis or extradural abscess formation. Obvious bone infection is of importance in half or more of the cases. Direct spread may also occur along a congenital petrous bone fissure, at the time of mastoid surgery, and in association with basal skull fracture.



a

b

Fig. 1. a, Example of dural reaction from specimen from Case 8. The membrane is folded upon itself with the exudative side innermost. ×15. b, Example of dural reaction from specimen of Case 7. Note the subdural exudate and the leptomeningeal reaction. ×33.

2. Retrograde venous extension. This may follow the course of afferent channels of a thrombosed lateral sinus. These possibilities have been outlined and explored by Courville and Nielsen (5).

3. Spread by metastasis. This mode of blood borne extension *à distance* has received some support.

The importance of the presence of intracranial purulent processes concomitant with otogenic subdural pus has received emphasis. Brain abscess, leptomeningitis, and major dural sinus phlebitis are the prominent lesions. Leptomeningitis has been considered responsible for the greatest percentage of deaths of patients with otogenic subdural abscess.

Subdural purulent collections secondary to accessory nasal sinusitis. From Bisgard's report of 1932 onward this form of the disease received increasing emphasis. In the vast majority of cases the subdural abscess follows frontal sinusitis, is less likely to be localized and is usually more fulminating than when of otogenic origin. Whether or not the acuteness or chronicity of the sinusitis is important in the pathogenesis of the subdural abscess remains undecided.

Five modes of spread of infection from the diseased sinus to the subdural space have been suggested:

1. Via local bony defects from erosion, osteomyelitis, or fracture. The association of subdural pus and extensive cranial osteomyelitis is not common, approximating 10 per cent. Extension of pus through the posterior wall of the frontal sinus with gross dural perforation occurs, but is a less common mechanism than in the otogenic abscesses.

2. Via vascular channels. This is probably the most important method of spread. It may occur in association with superior longitudinal sinus thrombosis or through the mucosal vein of the nasal sinus, thence via the dural sinus to the subdural space or cortex, traversing en route the diploic and emissary veins. In the majority of cases no visible bone or dural changes are found. Vascular mechanisms have been enlisted to explain distant and bilateral abscesses in the subdural space.

3. Via congenital bony defects adjacent to the infected focus.

4. Via a patent craniopharyngeal canal.

5. Via the perineural sheaths of the olfactory nerves.

The frequent association of other severe intracranial infectious processes with this form of subdural abscess is of vital importance and is similar to that discussed under the otogenic abscesses.

Subdural purulent collections secondary to trauma to the skull and brain. This group ranks third in importance in the incidence of subdural abscess. Indirect invasion rather than direct traumatic implantation has been considered the usual route of infection. The disease may occur after operative procedures have been performed.

The excellent analysis of Courville and Blomquist (6) deserves study.

Subdural collections secondary to diffuse leptomeningitis. Recent reports (16, 20) have directed attention to a special form of subdural collection which occurred as a complication of bacterial meningitis. The cases were found in infancy and early childhood incident to Hemophilus influenzae (B) and less often other meningitides, notably Diplococcus pneumoniae. The subdural fluid, of high protein content, was usually encountered bilaterally during the unsatisfactory course of a "bacteriologically cured" meningitis. The fluid was sterile in 80 to 85 per cent of these reported cases; but in the remaining percentage, positive cultures were obtained, and subsequent experience has shown that truly purulent collections do develop in these same circumstances.

Subdural collections due to miscellaneous causes. Courville (4) wrote that the subdural abscess which could occasionally be found secondary to a purulent rhinitis in infants and young children probably had a vascular pathogenesis similar, to the cases following sinusitis even though the frontal sinuses were rudimentary.

Subdural abscess following still more remote causes has been described.

ANALYSIS OF CURRENT CASES

Brief notes describing Case 13 from the current series of 16 consecutive cases emphasize the urgency of the majority of subdural purulent infections.

CASE 13. This 12 year old boy entered the hospital December 24, 1945. Frontal headache and fever accompanied by nausea and vomiting began 11 days before admission. Three days later generalized convulsive seizures began. Culture of cerebrospinal fluid was reported negative.

Upon admission the patient's temperature was 37.4 degrees C. He was somnolent with a "cracked pot" percussion note of the head. Kernig's sign was positive bilaterally together with a defect in ocular convergence. White blood count was 16,600. Lumbar puncture showed a pressure of 175 millimeters of water; 35 mononuclear cells; and a total protein of 85 milligrams per cent. Roentgenograms showed cloudiness of the accessory nasal sinuses.

At operation, pus under pressure was encountered beneath the dura mater in the right and left frontal regions and in the left temporal region. Culture of the pus contained micro-aerophilic Streptococcus viridans. On January 5, 1946, the ventricular system was shifted to the right, and bilateral papilledema and dysphasia developed. An additional collection of subdural pus was encountered in the left frontotemporal region. The last follow-up note was dated March 29, 1946, at which time electroencephalograms revealed a generalized and focal dysrhythmia. The patient was improving, but slight weakness in the right hand persisted.

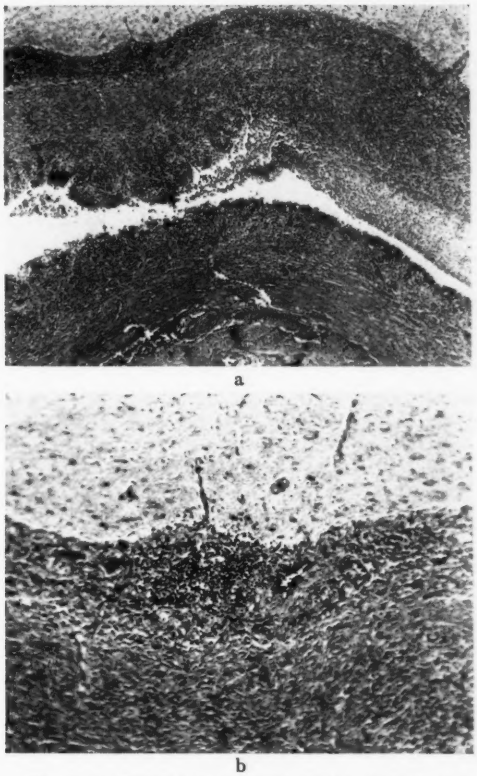


Fig. 2. a, Example of subdural exudate from Case 9. At the upper margin may be seen the dural membrane beneath which is the zone of subdural exudate, split in the middle by artefact. The exudate fuses imperceptibly with the leptomeningeal reaction. ×15. b, Example of the leptomeningeal reaction from the specimen above. Note the minimal cortical reaction. ×33.

Sinusitis was probably the source of the original infection in this case. The danger that this patient may have developed convulsive seizures is real.

The age of our patients ranged from 8 months to 46 years. There were 11 males and 5 females. The duration of acute symptoms

was limited to 8 weeks or less in 13 of the 16 cases. The longest history occurred in the case of traumatic osteomyelitis of 26 years' duration. The shortest history of 10 days occurred in a case which in its late stages was associated with a leptomeningitis.

Our attempt to uncover the primary infectious process and pathogenesis of the subdural pus revealed these probable causes in the 16 cases of this series: frontal sinusitis, acute or chronic, in 5 cases; otitis media, acute or chronic, in 5 cases; head trauma with osteomyelitis in 2 cases; acute leptomeningitis in 2 cases; and inconclusive evidence in 2 cases.

In 3 cases leptomeningitis was associated as a concomitant lesion (in 2 of these 3 cases it was probably the primary lesion). There were 3 examples of associated intracerebral abscesses, single and multiple. In a fourth case a large intracerebral projection from the subdural cavity was encountered. There were no examples of major sinus thromboses in the series.

In the series there were 3 examples of bilateral subdural collections of pus. In 10 patients the abscesses were unilateral. In 2 of the 10 unilateral cases the lesions were multiple, encapsulated collections.

Bacteriological studies were available in all but 1 case. In 10 of the 15 cases on which data are available, some form of the streptococcus was present either alone or with some other organism. This dominance of the streptococcus was previously recorded in a larger series (19).

In only 2 of the 16 cases was the diagnosis of subdural abscess made preoperatively. In 12 cases an intracranial infectious process was diagnosed. It was specified as a brain abscess in 9 of the 12 cases. In 1 case an intracranial neoplasm was suspected.

In 8 cases there was evidence of localizing motor weakness prior to admission, and 11 patients presented definite histories of convulsive seizures of some type prior to entry. Ten patients were febrile at the time of hospital entry, and 4 others had histories of fever during their illnesses before entry.

Certain important clinical findings in the 16 cases may be emphasized by the following: Altered consciousness was noted in 15 cases; papilledema in 10 cases; motor weaknesses in 12 cases; reflex alteration in 14 cases; signs of meningeal irritation in 10 cases; leucocytosis in 12 cases. Other findings occurred less consistently: for example, local head findings in 7 cases; Jacksonian seizures in 4 cases; visual field changes of localizing value in 3 cases; and other cranial nerve involvement in 6 cases.

Plain x-ray films of the skull were useful in localizing the purulent process in 4 cases. These were examples of focal osteomyelitis (Fig. 3).

An interesting feature which has received some attention by other authors is the spinal fluid findings associated with the disease. Ertl emphasized the predominance of lymphocytes over polymorphonuclear cells. He also noted a consistently elevated protein and negative cultures. We reviewed all the cases included in the literature which have been cited heretofore and included the case of Mallory. Our own cases lend support to the following opinion: It would appear that while an elevated protein (and pressure) may frequently be observed, the pleocytosis may vary as to number and cell type to such an extent as to make the finding of little diagnostic value. However, on the contrary, the consistent finding of sterile cultures in the spinal fluid is of importance. We recognize the occurrence of sterile leptomeningeal reactions beneath the areas of subdural purulent collections. Only when the barrier to the open subarachnoid space is broken will organisms be encountered in the spinal fluid examination. Of course, in those cases in which subdural abscess follows a leptomeningitis, notably Hemophilus influenzae type B, there may be a time when organisms can be recovered.

THE TREATMENT OF SUBDURAL ABSCESS

The history of the evolution of surgical treatment of this disease has been covered elsewhere. Post and Mollison recommended free drainage of the local pus combined with frequent lumbar punctures in the handling of such infections. Gardner argued against the early operative treatment, suggesting that a poorly localized process might be further spread. However, it has been well established that subdural pus may kill before it has any

semblance of encapsulation of surgical significance.

Bray and Haverfield recommended early external drainage of any suppurating frontal sinus to preclude the extension of infection to the bone or brain. We must add, however, that when dealing with cases of fulminating disease, temporizing with nasal surgery may cause the loss of important time. Ray and Parsons believed that in the face of frontal sinus infection the decision to remove the posterior sinus wall must not rest on finding grossly altered or softened bone. They advised evacuation of any extradural pus followed by the opening of the dura mater through a clean field and suggested that upon opening the dura mater an abscess might be overlooked due to gravitation of the pus to dependent areas. They advised the use of multiple bony openings and small rubber drains. Kubik and Adams recommended drainage of the abscess through an enlarged burr opening, and Courville (10) advised bilateral trephination should any uncertainty be present. Kahn recommended that the dura mater be opened through a clean field, combined with lumbar puncture to permit exposure of the reaches of the subdural space. Gross believed the bony removal must guarantee adequate drainage, and condemned primary scalp closure.

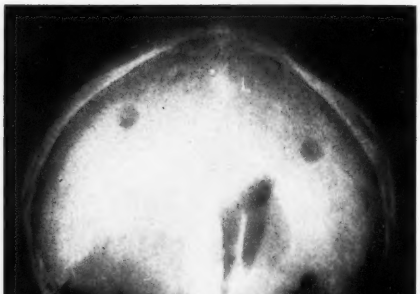
The advent of powerful antibiotics facilitated the treatment of subdural empyema. Probably the first use of penicillin, both systemically and by catheter, into the subdural space occurred in 1943 in the case reported by Schiller, Cairns, and Russell. These authors recommended the localization of the subdural pus by puncture through burr openings, aspiration of the pus, and intermittent irrigation with penicillin by indwelling catheter. It is significant that all cases of these authors in which penicillin was withheld or given only into the subdural space ended fatally. Additional reports of experience with drainage of the subdural space and the local use of penicillin came from Gross, Anderson, and Keith, who presented the largest successfully treated series known to the authors. Glass employed an osteoplastic flap in the treatment of the infection. The program of treatment outlined by Gurdjian and Webster incorporated the

Fig. 3. Example of the roentgenological findings in Case 11 of traumatic osteomyelitis of the frontal bone associated with subdural abscess.

principles of multiple trephination, drainage, and subdural antibiotic therapy.

Regional complications may for a time obscure the subdural lesion. The following findings should give warning: In the course of a relatively benign process such as otitis media, or sinusitis or even in the absence of active infection, a definite change in the clinical status of the patient is seen. Headache, often localized, is constant and may be severe and associated with nausea and vomiting. A change in the conscious state is invariable with marked irritability or definite stupor. Meningeal signs are most often present, papilledema is frequent, and localizing neurological findings are the rule in almost every case observed or reviewed. The course is rapid and requires therapy quickly. Leucocytosis is present, and the lumbar puncture findings have been discussed.

The two major diagnoses in differential consideration are brain abscess and longitudinal sinus thrombosis. Purulent leptomeningitis is usually recognized except in the late stages when the lesions may be coexistent, or, as mentioned previously, meningitis may be followed by the subdural abscess as the lethal



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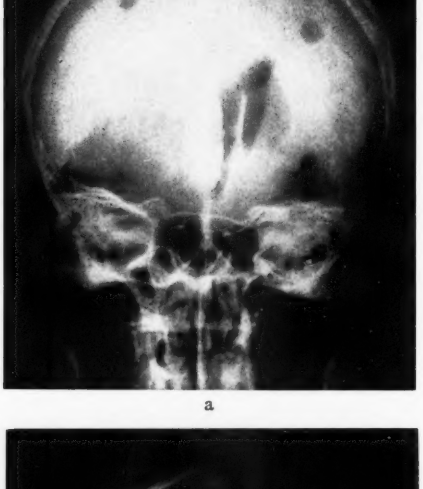


b

Fig. 4. a, Ventriculographic study in Case 14 before treatment, giving an example of the displacement of intracranial contents. b, Postoperative demonstration of ventricular realignment.

lesion. A diffuse purulent encephalitis may also cause difficulty in diagnosis.

In the case of brain abscess, the course is usually less fulminating, with fewer meningeal signs, less headache, and little fever. This lesion may coexist, but even so the subdural picture will overshadow that of the cortical lesion. Longitudinal sinus thrombosis frequently shows bilateral or alternating neurological signs. There is usually a septic temperature curve, meningeal signs are not as frequent or prominent, and there may be remissions. It must again be cautioned that this condition also may be found concomitantly with the subdural abscess.

Ventriculography may be helpful for localizing "silent" lesions such as distant brain abscesses or additional unsuspected loculations of subdural pus (Fig. 4). Such a study should be performed through openings placed in the area most remote from the suspected pus, and if pus should be encountered in the preparation for air studies, it is obvious that no needling should be done.

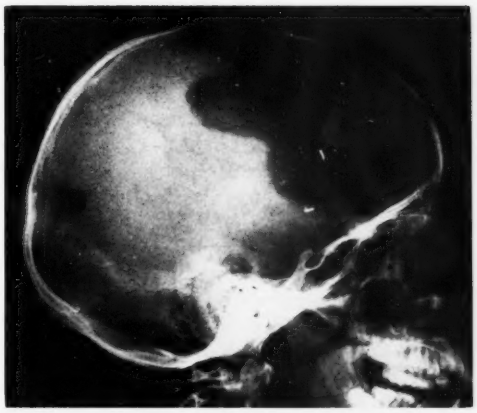
We offer the following suggestions, based on the cases handled personally and those reviewed at this center.

Once the subdural suppurative process has started, treatment must first and principally be directed toward this area. The site of primary pathology frequently needs no attention. We have had no patients, for example, that required mastoidectomy when otitis media or mastoiditis was the primary focus. Radical sinusotomy, particularly in the cases presenting a frontal sinusitis, may be required; and no hesitation should be felt in removing the apparently normal appearing posterior sinus wall. If the dura mater is found necrotic beneath the sinus or other primary focus and if the tension is high, rupture may occur. Further opening of the dura mater is then justified in the soiled field. If the dura mater is intact, then the judgment to open it may be dictated by an obvious alteration in the appearance or feel to the palpating finger. It may be edematous, more heavily vascularized, discolored, or show thinning or patches of epidural granulations. It may be necrotic, or it may be unchanged in appearance. Its tension may or may not be elevated upon palpation. In the absence of abnormal changes the decision must be based on a reasonable suspicion which has been aroused by suggestive history, physical findings, and course of the patient. It should be opened through a clean field.

The wound edges should be sealed off as nearly as possible, and bone should be removed at least widely enough to expose normal dura mater. The dural opening should allow ready introduction of a ribbon spatula and later several ¼ inch, soft Penrose drains. Lumbar puncture has been useful in permitting more thorough evacuation of the subdural space, but caution should be observed not to injure the limiting membranes about the periphery of the abscess. We have found, however, that many septa which at first glance might seem to be the abscess wall were found, particularly at second stage operations, to be sealing off loculations of exudate which required drainage. These septa then must be broken down. We have had more success with wide bony removal rather than with multiple burr openings in providing drainage (Fig. 5). The main point to emphasize is that the roof of the abscess must be lifted off, and all tongues and reaches of the pus must be drained and irrigated. The inner, cortical wall of the abscess must not be disturbed.

We believe that local penicillin (500 units per c.c.), instilled daily by small catheters running in the Penrose drains and incorporated in the dressings, is beneficial. The dressings are time-consuming and require the observance of strict aseptic precautions, but such effort is well rewarded. We believe that the value of penicillin certainly depends upon the susceptibility of the organism in question, and such sensitivity tests should be run during the course of therapy as long as positive culture data are obtained. We do not stop systemic penicillin until all wounds are well healed, even though the temperature has been normal for some time. This prolonged application is particularly justified where any bony infection is, or has been, present.

The wounds are allowed to heal from the base. In the early postoperative weeks we strongly advise daily or, if necessary, twice daily, lumbar cerebrospinal fluid drainage. This is best done at the time of each daily dressing to allow the extent of the abscess cavity to be well visualized and made accessible to the instilled medications. We do not hesitate to perform further stages of bone removal to unroof the cavity where loculations



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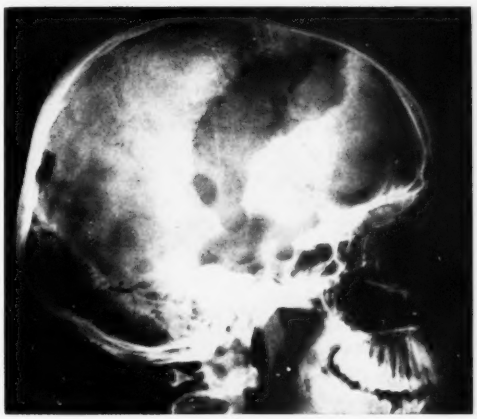

b

Fig. 5. Examples of the extent of bone removal in the complete unroofing of subdural exudates in, a, Case 12 and, b, Case 13.

are inaccessible. We have yet to find the intrathecal use of penicillin necessary in this type of infection. Sulfonamide therapy must be individualized.

It is unwise to demand adherence to a fixed routine. The best surgical principles must be served at all times, and each case will present peculiar problems which require special consideration.

RESULTS

Seven of the 16 patients died as a direct result of intracranial infection. Of the 2 patients not treated surgically, one died of a diffuse leptomeningitis and the other from

brain stem hemorrhages. Four of the 5 fatal cases in which operation was done had surgically unapproached intracranial purulent collections, subdural as well as intracerebral. There was no autopsy on the fifth patient. Similar to the experience of Schiller and associates, our survey revealed that 6 of the 7 deaths occurred before the advent of penicillin. However, of the surviving patients, 3 received no chemotherapy or antibiotics. No patient survived who was not given a satisfactory evacuation and drainage of the purulent collection, irrespective of the antibacterial medications administered.

We had no cases of subdural abscess between 1939 and 1945 when free use of penicillin came into being. There have been 7 cases since 1945. We do not believe the incidence of subdural abscess has been reduced since the free use of antibiotics, and there is suggestive evidence from our series that its percentage incidence has been increased. This is not to detract, however, from the improved results in the treatment of any given case by the use of antibacterial medication, including now the newer antibiotics.

The complications of the adequately treated case include the cranial defects which may be repaired after a suitable lapse of time. Convulsive seizures have been distressingly persistent and have occurred as a long term complication of 4 of our cases. In 3 of our patients who survived to leave the hospital, the follow-up has been incomplete, and it is highly possible that 1 or more of these may have suffered from convulsive seizures. Of the 4 patients with known convulsions, only 1 developed fits after her treatment, in contrast to the majority of patients with convulsions in their preoperative history. This coincides with the experience of Gurdjian and Webster.

REFERENCES

1. Anderson, F. M. Subdural empyema secondary to frontal sinusitis. Ann. Otol. Rhinol., 1947, 56: 5–17.
2. Bisgard, C. V. Empyema of subdural space. Canad. M. Ass. J., 1932, 26: 205–207.
3. Bucy, P. C., and Haverfield, W. T. Cranial and intracranial compiications of acute frontal sinusitis. J. Am. M. Ass., 1940, 115: 983–991.
4. Courville, C. B. Subdural empyema secondary to purulent frontal sinusitis; clinicopathologic study of 42 cases verified at autopsy. Arch. Otolar. Chic., 1944, 39: 211–230.
5. Courville, C. B., and Nielsen, J. M. Fatal complications of otitis media. Arch. Otolar. Chic., 1934, 19: 451–501.
6. Courville, C. B., and Blomquist, O. A. Traumatic pachymeningitis interna and subdural abscess with special reference to pathogenesis and pathology. Arch. Surg., 1941, 42: 890–908.
7. Ertl, E. E. Ein Beitrag zur pathologischen Anatomie, Diagnostik und Therapie der otogenen Pachymeningitis interna infectiosa. Arch. Ohr. &c. Heilk., 1941, 149: 119–155.
8. Gardner, W. J. Subdural abscess; its relation to sterile purulent leptomeningitis. Ohio M. J., 1933, 29: 235–238.
9. Glass, R. L. Osteoplastic flap method in the treatment of subdural abscess. J. Neurosurg., 1947, 4: 391–393.
10. Gross, S. W. Osteomyelitis of frontal bone and subdural empyema with recovery. Am. J. Surg., 1946, 71: 828–831.
11. Gurdjian, E. S., and Webster, J. E. Modern surgical treatment of acute subdural abscess. Arch. Surg., 1948, 57: 411–426.
12. Kahn, E. A. Brain abscess. Surgical Treatment of the Nervous System. Pp. 88–90. Edited by Bancroft, F. W., and Pilcher, C. Philadelphia: J. B. Lippincott Co., 1946.
13. Keith, W. S. Subdural empyema. To be published.
14. Kubik, C. S., and Adams, R. D. Subdural empyema. Brain, Lond., 1943, 66: 18–42.
15. Mallory, T. B. Subdural abscess, Cabot case 26351. N. England J. M., 1940, 223: 340–343.
16. McKay, R. J., Jr., Morissette, R. A., Ingraham, F. D., and Matson, D. D. Collections of subdural fluid complicating meningitis due to Haemophilus influenzae (type B). N. England J. M., 1950, 242: 20–21.
17. Post, H. W. A., and Mollison, W. M. Subdural abscess following operation on mastoid process; recovery. Guy's Hosp. Rep., Lond., 1926, 76: 479–481.
18. Ray, B. S., and Parsons, H. Subdural abscess complicating frontal sinusitis. Arch. Otolar., Chic., 1943, 37: 536–551.
19. Schiller, F., Cairns, H., and Russell, D. S. Treatment of purulent pachymeningitis and subdural suppuration with special reference to the use of penicillin. J. Neur., Neurosurg. Psychiat., 1948, 11: 143–182.
20. Smith, M. H. D., Dormont, R. E., and Prather, G. W. Subdural effusions complicating bacterial meningitis. Pediatrics, 1951, 7: 34–43.

SURGERY IN PREMATURE BABIES

Observations from 159 Cases

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DURING recent years there has grown in the minds of all physicians the realization that infants and small children cannot be treated surgically simply as diminutive adults, but must be handled with great care and with specially designed operative techniques. Particularly has it become obvious that surgical treatment of premature babies demands even more delicate supervision and consideration than is required for their full term brothers and sisters.

During the period from 1936 through 1951, 159 premature infants were operated upon at the Children's Hospital of Boston. Not all of these diminutive patients were actually premature in the sense that their period of gestation was unduly short nor did all of them weigh less than 5 pounds at birth. However, all of the babies weighed 5 pounds or less at the time of their operation, and hence have been regarded as being "premature." The experience gained in the operative treatment of these infants forms the basis for this report.

As soon as a baby has been born and the umbilical cord severed, he ceases to exist on maternal support and suddenly must function for himself as a complete and separate entity. In a matter of seconds, tremendous physiological changes take place which require enormous and quick readjustments in several organs and systems of the body. A full term infant only occasionally experiences trouble in making these rapid transitions, but an anatomically and physiologically immature human, born before completion of his period of development, almost invariably encounters some difficulty. If to this existing hazard there is added some major congenital malformation requiring surgical correction, the combination of obstacles presented to the premature infant may be insurmountable. However, if such infants are given prompt and efficient help, many of them can be tided through their trials and can be salvaged as normal and healthy children.

Before listing the surgical principles which have been found to be important in the care of the premature baby, a brief review of neonatal physiology is pertinent, placing special emphasis on the physiological inadequacies and limitations occurring as a result of prematurity. For a complete review of this subject the reader is referred to the excellent monograph *The Physiology of the Newborn Infant* by Smith, from which the authors have derived much of the information summarized herewith.

From the Children's Hospital and the Harvard Medical School.

PHYSIOLOGY OF THE PREMATURE CHILD

There are many items of importance which could be rightfully considered in a discussion of the physiology of prematures; only those will be presented which are particularly relevant to surgical management of these tiny patients.

Body temperature and metabolism. While the body weight of a normal full term infant comprises about 5 per cent of that of the average adult, the body surface area comprises approximately 15 per cent. In the premature infant, the body surface is proportionately even greater and is poorly protected because of the paucity of insulating subcutaneous fat, the lack of vasomotor control, and the inadequacy of sweating and shivering reactions. Concurrently, the body production of heat is at a low level. In combination, these factors make the premature infant extremely susceptible to variations in environmental temperature, from which changes he must be shielded temporarily.

Respiratory system. When the respiratory minute volume is computed on a basis of relative body surface area, the figures obtained for premature and full term infants approxi-

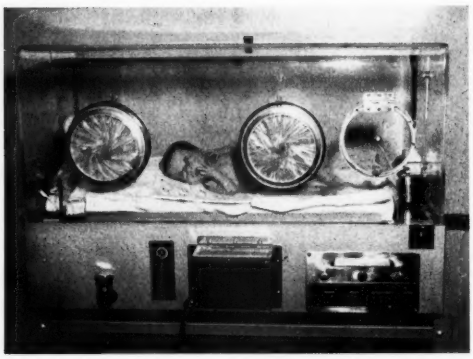

Fig. 1. Incubator unit (Isolette) which is extremely useful in the care of the premature baby. By automatic controls the atmosphere within the unit can be kept at a constant temperature and humidity. Oxygen can be introduced into the plexiglass enclosure. Side ports allow introduction of nurse's or doctor's hands for handling the baby.

mate those obtained for adults. However, this equality is accomplished by the premature infant at the expense of a vastly greater respiratory effort, indeed to such an extent that only minimal respiratory reserve remains. The respiratory movements of the newborn are almost entirely diaphragmatic. If these are hampered by the presence of abdominal distention, by a diaphragmatic hernia, or by conditions in the lungs such as atelectasis or pneumonia, the premature infant has little or no respiratory reserve to fall back upon and may succumb because of the overwhelming combination.

The breathing of a premature infant is frequently jerky or periodic. This irregularity is generally innocuous, but in some instances it may be due to mild anoxia and will be found to disappear when oxygen concentration above that of room air is given.

Fig. 2. Baby with esophageal atresia and tracheoesophageal fistula who weighed 4 pounds, 3 ounces at the time of thoracic operation for closure of the fistula and primary anastomosis of the esophageal ends. Photograph 2 weeks after operation. Child is in excellent health 2 years later.

While the brain of a small baby will survive more severe episodes of anoxia than will that of an adult, anoxia must be avoided or minimized insofar as possible.

Cardiovascular system. The blood volume of a newborn is proportionately similar to that of an adult, amounting to about 8 per cent of the body weight, but is subject to alterations as great as one-fourth to one-third of its total amount, depending upon whether the umbilical cord is clamped before or after pulsations have ceased within it.

While variations are frequently encountered, compared to a full term infant, the premature baby tends to have a slightly higher pulse rate, a lower blood pressure, a lower erythrocyte count, a lower hemoglobin level; yet to meet the demands of his relatively larger body surface area he is required to have a greater cardiac output. As with the respiratory system, this relatively greater expenditure is made at the expense of cardiovascular reserve. This depleted reserve, coupled with a lack of peripheral vasomotor control, makes the premature infant particularly susceptible to alterations in blood volume, such as occur in blood loss, shock, or overhydration.

The plasma protein levels of premature infants are universally low. This deficiency affects the globulin slightly more than the albumin fraction. The resulting diminution of plasma osmotic pressure, in combination with increased permeability of the capillary beds facilitates the formation of edema. A low globulin level, coupled with the initially low leucocyte counts which are generally encountered, make premature infants particularly susceptible to infections.

Blood coagulation is usually normal or slightly prolonged at birth, but by the third day there may develop a serious hemorrhagic tendency. This is due to a transient hypoprothrombinemia, which can be prevented by the parenteral administration of vitamin K.

Alimentary system. The gastrointestinal tract of a newborn shows a greater development of secretory and absorbing surfaces than

of supporting musculature. Hence the bowel is especially prone to distention and may rapidly undergo necrosis and rupture.

The output of hydrochloric acid by the stomach is strikingly high for a short period after birth, but within a few days becomes quite low. The high value may be an etiologic factor in the formation of perforating peptic ulcer of the newborn, although brain damage is often considered to be the primary cause.

Enzymes adequate for the digestion of all simple foods, excluding starches, are present at birth, although fat also is usually poorly tolerated by premature infants.

While the liver is sufficiently developed in the full term infant for adequate function, the greater intensity and duration of icterus neonatorum in the premature has been thought to indicate mild impairment of liver function.

The vitamin and mineral reserves of the newborn are usually adequate unless maternal stocks previously available to it were extremely meager. By the administration of vitamin C, Levine, Gordon, and Marples have shown that the otherwise incomplete metabolism of certain amino acids in premature infants may be corrected. Integrity of intercellular tissue and promotion of wound healing are also favorably influenced by administration of this vitamin.

Adrenal glands. Unless the adrenal glands are damaged by hemorrhage, their function is usually sufficient to meet most stresses of neonatal life. In rare instances, however, as a result of chronic infection and repeated surgery, poor adrenal response has been observed, as indicated by high eosinophil counts. Under such circumstances, the administration of ACTH, cortisone, or adrenal cortical extract has appeared to produce clinical improvement.

Urinary system. At birth the kidneys of premature infants are far from being completely matured. Anatomically this is recognizable by persistence of fetal lobulation and by the lack of full glomerular development. Physiological immaturity is shown by the limited powers of urinary concentration, by low clearance levels of urea, sodium, and chloride, and by frequent albuminuria. Despite a mild metabolic acidosis, due to an increase of inorganic and organic acids in the blood of the premature infant, the blood hydrogen ion concentration is at essentially normal levels, averaging 7.4. This *p*H is maintained by a compensating low blood carbon dioxide content (22 mEq. per liter). Therefore, if dehydration results from abnormal fluid loss (such as occurs with diarrhea or vomiting) the premature infant is particularly liable to develop serious acidosis.

Fig. 3. Baby who weighed 4 pounds, 4 ounces at the time of intrathoracic operation for correction of esophageal atresia and tracheo-esophageal fistula. Repair by division of fistula and primary anastomosis of esophageal ends. Photograph taken 6 months after operation to show excellent condition of the child. He is in excellent health at 7 years of age.

PRINCIPLES OF SURGICAL CARE FOR PREMATURE INFANTS

From the bitter experiences gained from many fatalities or from the development of serious complications when surgically treating premature babies, we have now come to regard

a b

Fig. 4. a, Photograph of baby weighing 2 pounds, 15 ounces at the time of operative correction for esophageal atresia and tracheo-esophageal fistula. Intrathoracic, retropleural operation by division of the fistula and primary anastomosis of esophageal ends. b, Photograph of child 13 months later. No difficulty in swallowing.

Fig. 5. Photograph of baby weighing 4 pounds, 10 ounces who had hypertrophic pyloric stenosis. Baby successfully treated by Ramstedt pyloromyotomy.

the following items of great importance in the handling of these small and fragile patients.

Warm, constant temperature environment. When a premature baby requiring surgery is admitted to a hospital, he usually has been transported a considerable distance from the referring maternity hospital. Despite precautions taken during this trip, he frequently has been exposed to suboptimal temperatures, and his body temperature is very low. There should be available an incubator which provides an adjustable, constant temperature and humidity; for this purpose we have found the "Isolette" to be most useful. In addition to its excellent mechanical controls, it affords good visibility, ease in handling the patient, and has adequate provision for the entrance of intravenous and suction tubes. The infant should be immediately transferred to such an incubator, the temperature of which is kept at 90 to 95 degrees F. until his body temperature reaches 98 degrees F. The incubator thermostat is then adjusted to a slightly lower figure (around 85 degrees F., depending upon the infant's size) and the baby is allowed to establish his own temperature level. Frequently this is slightly lower than 98 degrees F., which is not disadvantageous, and may be even advantageous since body tissue metabolic demands are somewhat reduced thereby.

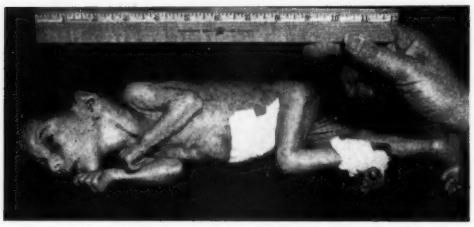

Fig. 6. Baby weighing 2 pounds, 6 ounces, having duodenal atresia. The length of the entire abdomen is but 2½ inches. The child was successfully treated by isoperistaltic retrocolic duodenojejunostomy. Child in excellent health 2 years later.

Attention to the respiratory system. Since most of these infants have a congenital condition which either directly or indirectly diminishes respiratory reserve, it is essential that the respiratory system be given all possible assistance. This is partially accomplished by the administration of oxygen. Other methods of assistance might include the alleviation or prevention of intestinal distention, suction removal of excess tracheal mucus, treatment of pneumonia, or the administration of whole blood to increase the oxygen-carrying capacity of the blood. In addition to raising any low hemoglobin level, transfusions have the possible value of supplying carbonic anhydrase, an enzyme invariably diminished in the blood of the premature infant.

When any element of tracheal obstruction is present, a supersaturated moist atmosphere is usually of benefit, and may be accomplished by employing a nebulizer (1) for spraying droplets into the enclosure within the incubator.

Isolation. The premature baby is acclimatized to the cushioned existence of intrauterine life, and the less he is handled, the better. By placing the infant under full vision in an Isolette, he can be watched frequently and yet he is reasonably well protected from infection to which he is so susceptible. The baby should be handled just as little as possible; only the most necessary diagnostic or therapeutic manipulations should be allowed. Temperature taking, weighing, injections, or cleansing are kept to the barest essentials. No clothing is put on the baby; diapers are simply laid under the buttocks and are replaced as required.

Preoperative care. All newborn infants are given vitamin K (hykinone 2.5 mgm., subcutaneously daily) before and after operation. Penicillin is also routinely given prophylactically to guard against infection. Atropine (0.065 mgm.) is administered subcutaneously approximately 1 hour prior to operation, but no sedative is given. Ideally the premature infant should be transported from the ward to the operating room in an incubator, but this

is usually impossible because of the incubator's permanent electrical and oxygen attachments. We, therefore, move our infants in a warmed bassinette covered by a plexiglass dome. Oxygen from a portable tank is supplied during transportation.

After everything has been made ready in the operating room, the baby is placed on a covered hot water bottle on the operating table. The extremities are swathed in cotton sheet-wadding to preserve body heat. In all premature infants, with the possible exception of those with hypertrophic pyloric stenosis, blood is required during the operative procedure. Accordingly, a "cutdown" is performed upon a median ankle vein or an antecubital arm vein. The "cutdown" is usually done under local anesthesia as the patient is being prepared.

Anesthesia. Probably the safest, but by no means the most satisfactory anesthesia, is local procaine infiltration of the wound area plus oral sedation by means of a brandy nipple. Local anesthesia, however, has serious limitations in the presence of abdominal distention or when a chest must be opened. We now believe that general anesthesia given by a competent anesthetist is quite safe and is very satisfactory. Cyclopropane is the agent of choice since it affords easy induction, good relaxation, rapid recovery, and permits the continual administration of oxygen in high concentration. Intratracheal intubation should never be used except in an emergency; it is too apt to give dangerous postoperative laryngeal edema. A premature infant's lungs are friable and easily damaged by overaeration. With an intratracheal tube in place it is too easy for an anesthetist to overdistend and rupture pulmonary alveoli. The leaks around even the snuggest face mask almost entirely eliminate this danger, yet a tightly fitting mask permits satisfactory positive pressure when required.

Operative techniques. The shorter the length of time the premature infant is subjected to anesthesia and operative trauma, the better are his chances for survival. The surgeon must act swiftly and the procedure performed must be as simple as possible. Haste, however, should not permit rough or poor surgical technique. Extensive explorations should be

Fig. 7. Baby weighing 4 pounds who had annular pancreas with duodenal stenosis, accompanied by gastric dilatation and rupture. Treated by closure of gastric rent and by duodenojejunostomy. Child in good health 1 year later.

avoided. The corrective procedure must not be chosen solely because it gives a short operating time; it must be one which will give adequate relief.

Sutures must be very fine. We generally employ No. 00000 silk on atraumatic needles, or catgut no larger than No. 0000 chromic with swaged-on needles. Wounds must be cleanly incised and must be made with sound anatomical principles in mind. Closure is carried out in layers with small, fine, interrupted silk sutures. Retention sutures are not required in the abdominal wall. All tissues must be handled extremely gently, and the inclusion of large bites of tissue in sutures must be avoided.

Wound dressings. Bandages should be securely but loosely applied. Adhesive tape swathing the abdomen or chest may seriously hamper respiratory movements. When applied loosely, elastoplast makes a very satisfactory covering for a dressing because of its

Fig. 8. Child who weighed 3 pounds, 7 ounces, having duodenal obstruction from an annular pancreas. Treated by duodenojejunostomy. Photograph 1 month later. Note excellent healing of wound. Child in good health 4 years later.

Fig. 9. Baby weighing 3 pounds, 12 ounces, having duodenal obstruction from an annular pancreas and also malrotation of the colon and intestines. Treated by Ladd's procedure for correction of malrotation and by duodenojejunostomy. Child in excellent health 2 years later.

ability to stretch. Any rubber drain or tube which has been left in a wound must be firmly secured. The premature infant, despite his apparent weakness, has demonstrated diabolical cunning and considerable skill in removing gastrostomy tubes and chest catheters.

Minimal laboratory studies. Not only is it desirable to disturb the premature infant as little as possible, but the hematological or biochemical procedures which can be done are limited by the difficulties of obtaining adequate blood samples. We have seen more premature babies damaged than have been helped by overenthusiastic efforts to "find out about the blood chemistries." The baby must not be mauled by attempting to withdraw blood for some esoteric chemical determination, the report of which has little to do with guiding the subsequent therapy. Furthermore, the infant's condition is so subject to rapid change that by the time results are received from the laboratory they often no longer represent the status of the child. For the premature baby it is more rewarding to rely upon one's "clinical" judgment in evaluating the condition of the baby; only rarely need laboratory aids be employed.

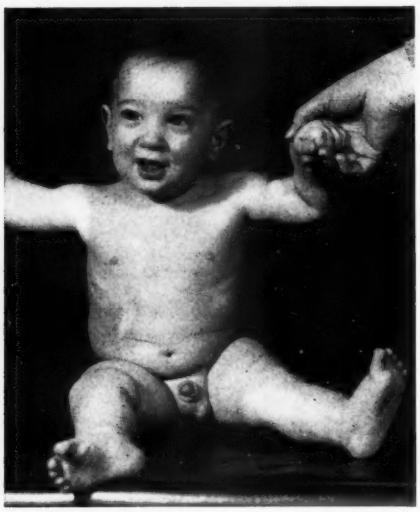

Fig. 10. Child who weighed 2 pounds, 15 ounces at the time of operation for duodenal atresia which was treated by duodenojejunostomy. Photograph taken 1 year later showing excellent health of the subject.

Preset 24 hour limitation on parenteral fluids. Because of the premature infant's diminished cardiac reserve, his tendency to formation of edema, and his inability to excrete large volumes of urine, he is particularly susceptible to overhydration. Once an intravenous needle is in place, there is a strong temptation to run in just a little more fluid than had been previously decided upon; this is very apt to be a lethal act. We have seen scores of infants die because of excessive administration of parenteral fluid; we do not remember seeing one die because of dehydration. We have therefore developed a firm policy of presetting the total amount of parenteral fluid which shall be given in a 24 hour period, and this must not be exceeded. For 4 or 5 days after surgery, a baby who is taking nothing by mouth should not be given parenterally more than 30 cubic centimeters per pound per 24 hours. This total must not be given at one sitting but should be divided into 2, or preferably 3, administrations. As a practical matter, it is always preferable to keep these babies on the "dry" side during their early postoperative period. It is much better to prevent than combat edema of the lungs and brain. For guiding any alterations in the amounts of fluid which are to be given, the most reliable signs are the turgor of the skin, the tension of the anterior fontanelle, the change in body weight, number of urinations, and the presence or absence of edema. Toward the end of the first postoperative week more liberal amounts of fluids can be given, the problems of fluid therapy being considerably eased when the child can take adequate nourishment by mouth.

Frequent use of intravenous blood, plasma, or albumin. When there is any anemia, blood transfusions increase the efficiency of the premature infant's circulatory and respiratory system; certainly any deficiencies in hemoglobin levels should be promptly corrected.

Infusions of blood, plasma, or human albumin elevate plasma protein levels, and thus prevent or diminish the formation of edema. While it is highly desirable to maintain adequate serum protein levels in all patients, it is of particular importance in those who have had intestinal anastomoses, since the return of gastrointestinal function may be greatly delayed by the presence of swelling at the suture line. Because the elevations in blood protein are usually temporary, repeated small infusions are not only safer, but are of greater benefit than are single infusions of larger volume. We have found that injections of human albumin (salt-poor variety) are extremely useful and have come to use them in all premature infants for whom major surgery has been performed. This material can be diluted with water or glucose solution so that the albumin concentration approximates that in normal plasma. If dehydrating effect is desired—which is so often the case—the material can be given intravenously, 3 or 4 times normal plasma albumin concentration, injecting 2 cubic centimeters per pound of body weight.

Avoidance of parenteral saline solution. The promiscuous use of parenteral solutions containing electrolytes is to be avoided in premature babies. Only very small amounts of salt can be excreted by the premature infant's kidneys. It is very easy to produce harmful edema if unneeded salt is supplied to the body. In certain cases, this may be a very serious, irreversible, and even fatal complication. For these reasons salt solution should very rarely be given to premature infants. When treating severe acidosis, sodium bicarbonate or sodium lactate solutions may be required, but in most instances the correction of dehydration by the administration of 10 per cent dextrose in water will effect an improvement in the electrolyte pattern. As soon as fluid and milk can be tolerated by the gastrointestinal tract, the infant usually rapidly corrects any chemical imbalance by himself.

Fig. 11. Baby who weighed 4 pounds, 15 ounces, having stenosis of upper ileum. Treated by sidetracking ileo-ileostomy. Child in excellent health 1 year later.

Intermittent intestinal aspiration. Premature infants withstand poorly long continued gastric intubation. Their pharyngeal and esophageal mucosa is delicately thin and is easily traumatized. Of greatest importance is the fact that a tube which is left long in the pharynx is very apt to initiate obstructing edema of the glottis and larynx. When premature infants have conditions requiring gastric decompression, it is best to avoid an inlying catheter and to accomplish deflation of the stomach by passing a small catheter (No. 8 or 10 French urethral catheter) into the stomach every 3 or 4 hours, emptying the stomach, and then immediately withdrawing the tube.

Gavage feedings. Premature infants generally have poor sucking action and are all too apt to tire themselves if made to suck from a nipple. It is, therefore, better to feed them by gavage to eliminate this expenditure of energy. When the tube is inserted, any fluid or air should be sucked out of the stomach to guard against overdistension; the formula is then

Fig. 12. Baby weighing 2 pounds, 11 ounces, having multiple atresias of the ileum. Treated by excision of the atretic areas and side-to-side anastomosis of the remaining loops. Photograph taken 1 month later. Note satisfactory condition of wound. Child in excellent health 4 years later.

a

b

Fig. 13. a, Baby being placed on operating table. Child eighing 4 pounds and having an omphalocele. Treated by two stage closure of the abdominal wall defect. b, Photograph at 1 year of age showing satisfactory condition of abdominal wall. There is a good muscular and fascial repair.

TABLE I.—PATHOLOGY AND RESULTS OF THERAPY IN 159 PREMATURE INFANTS (5 POUNDS OR LESS) UNDERGOING SURGERY

January 1, 1936 through December 31, 1951

Diagnosis	No. of cases	Survived and discharged from hospital
Atresias		
Esophageal	51	17
Duodenal	11	6
Jejunal	6	3
Ileal	7	3
Imperforate anus	11	7
Stenoses		
Pyloric (hypertrophic)	25	23
Duodenal	4	4
Jejunal	1	1
Ileal	2	1
Annular pancreas	7	6
Obstruction from malrotation	5	1
Obstruction of jejunum by bands	1	1
Exploration for ? obstruction	3	3
Intussusception	1	1
Meconium ileus	6	0
Perforated duodenal ulcer	1	0
Omphalocele	6	5
Ruptured omphalocele	4	0
Diaphragmatic hernia	3	1
Strangulated inguinal hernia	2	2
Sacrococcygeal teratoma	2	2
Totals	159	87

Survival rate—54 per cent

slowly instilled, the tube withdrawn, and the child allowed to drop off to sleep.

Because of the premature infant's intolerance to fat, we customarily employ either high protein feedings or breast milk.

General postoperative care. It is frequently forgotten that these small infants suffer pain which may seriously hinder respiratory movements and may prevent much needed rest. It must be remembered too that sometimes the infant is so exhausted that he cannot cry to let you know his plight. Very small doses of phenobarbital (2 to 6 mgm.) given by mouth or subcutaneously every 6 to 8 hours are often beneficial, but careful watch for evidence of oversedation must be maintained. Extreme restlessness sometimes occurs in these infants following surgery, and may be harmful because of the resulting increased metabolic demands of the body. Phenobarbital is also very effective in such instances.

Following an operation of any magnitude, complications can occur so quickly in these small patients that it is essential to provide constant nursing care. Complications are predominantly apt to be respiratory in nature. Because of this, a suction apparatus must be constantly available. It is well to keep an

infant's laryngoscope with suitable intratracheal tubes close by, ready to be used in the event of an emergency. Respiratory stimulants such as coramine or caffeine and sodium benzoate are only occasionally of value in acute respiratory distress. Small repeated doses of them may be of definite value if the infant's respiratory rate is very slow or irregular and is unaltered by the administration of oxygen.

Antibiotics are almost routinely given after surgery. Penicillin (30,000 units per 24 hours) and streptomycin (10 mgm. per pound per 24 hours) are the agents of choice, because of their effectiveness, low toxicity, and availability for intramuscular administration. Other antibiotics such as terramycin and aureomycin may be effectively given by mouth late in the postoperative period, but because of their tendency to produce thrombosis, their intravenous use is to be avoided whenever possible. One complication of antibiotic therapy peculiar to infants is the development of thrush. Most antibiotics enhance the growth of monilia; their administration must be stopped should thrush appear. In this event, if bacterial infection must still be combatted, the sulfonamides are of value. Sulfadiazine (¼ gr. per pound per 24 hours) is most useful and has a wide range of antibacterial activity but its administration must be carefully watched because of possible damage to the kidneys.

CLINICAL MATERIAL AND RESULTS OF SURGERY

During the past 16 years 159 premature infants have been operated upon by members of the attending and resident staff on the general surgical service of the Children's Hospital of Boston. At the time of surgery, all infants weighed 5 pounds or less. The average weight of all infants was 4 pounds, 3 ounces. Ten infants weighed less than 3 pounds; 7 of these survived. The smallest patient to survive was a female weighing 2 pounds, 6 ounces, who had duodenal atresia and was treated by a duodenojejunostomy. Out of the entire group of 159 patients, 87 survived and were discharged from the hospital, a survival rate of 54 per cent. In the last year of the study (1951) there were 19 prematures, with survival of 15, a recovery of 79 per cent. It is of interest that in the entire series there was only 1 death on the operating table.

Fig. 14. Child weighing 3 pounds, 7 ounces, having a sacrococcygeal teratoma. After removal of the mass, the baby weighed 2 pounds, 11 ounces. Child in excellent health and without evidence of recurrence 2 years later.

The disease conditions present in the 159 infants and the results obtained following surgery are listed in Table I. It is seen that the most frequent diagnoses were congenital malformations of the gastrointestinal tract. Of these, esophageal atresia with tracheo-esophageal fistula was the most common, followed next in frequency by congenital hypertrophic pyloric stenosis. In 46 infants (28.9 per cent) multiple congenital anomalies were found. The most frequent complicating anomaly amenable to surgery was malrotation of the bowel. This occurred in 9 patients.

Most of the infants in this series were newborns, and were operated upon during the first few days of life. Those with pyloric stenosis and other incomplete intestinal obstructions, however, were operated upon later, usually between the second and fourth weeks of life. The average age at operation for all patients was 10 days. Ninety-one males and 68 females were operated upon but this male predominance is almost entirely attributable to the high ratio of males to females to be expected in the group of 25 cases of hypertrophic pyloric stenosis (20 males: 5 females). With other diagnoses, sex distributions were approximately equal.

A total of 212 operations of various sorts were performed. Of the anesthesias given, cyclopropane was employed 125 times, local

TABLE II.—LIST OF 87 PREMATURE INFANTS WHO HAVE SURVIVED SURGICAL PROCEDURES*

Case No.	Diagnosis	Weight at operation lb.	oz.	Operation
1	Esophageal atresia	3	12	Partial repair of anomaly†
2	Esophageal atresia	3	12	Partial repair of anomaly†
3	Esophageal atresia	4	8	Partial repair of anomaly†
4	Esophageal atresia	4	11	Partial repair of anomaly†
5	Esophageal atresia	4	11	Partial repair of anomaly†
6	Esophageal atresia	4	13	Partial repair of anomaly†
7	Esophageal atresia	2	15	Esophageal anastomosis
8	Esophageal atresia	4	3	Esophageal anastomosis
9	Esophageal atresia	4	4	Esophageal anastomosis
10	Esophageal atresia	4	7	Esophageal anastomosis
11	Esophageal atresia	4	8	Esophageal anastomosis
12	Esophageal atresia	4	8	Esophageal anastomosis
13	Esophageal atresia	4	12	Esophageal anastomosis
14	Esophageal atresia	5	0	Esophageal anastomosis
15	Esophageal atresia	5	0	Esophageal anastomosis
16	Esophageal atresia	5	0	Esophageal anastomosis
17	Esophageal atresia	5	0	Esophageal anastomosis
18	Duodenal atresia	4	1	Gastrojejunostomy
19	Duodenal atresia	2	6	Duodenojejunostomy
20	Duodenal atresia	2	15	Duodenojejunostomy
21	Duodenal atresia	3	3	Duodenojejunostomy
22	Duodenal atresia	4	8	Duodenojejunostomy
23	Duodenal atresia	4	14	Duodenojejunostomy
24	Jejunal atresia	3	9	Jejunoileostomy
25	Jejunal atresia	4	3	Jejunoileostomy
26	Jejunal atresia	4	7	Jejunoileostomy
27	Ileal atresia	2	14	Resection; ileoileostomy
28	Ileal atresia	4	0	Mikulicz anastomosis
29	Ileal atresia	4	4	Ileocolostomy
30‡	Imperforate anus	2	9	Colostomy
31	Imperforate anus	3	5	Colostomy
32	Imperforate anus	3	6	Colostomy
33	Imperforate anus	4	1	Proctoplasty
34	Imperforate anus	4	10	Proctoplasty
35	Imperforate anus	4	12	Proctoplasty
36	Imperforate anus	4	15	Proctoplasty
37	Pyloric stenosis	3	3	Pyloromyotomy
38	Pyloric stenosis	3	10	Pyloromyotomy
39	Pyloric stenosis	3	14	Pyloromyotomy
40	Pyloric stenosis	4	3	Pyloromyotomy
41	Pyloric stenosis	4	4	Pyloromyotomy
42	Pyloric stenosis	4	4	Pyloromyotomy
43	Pyloric stenosis	4	6	Pyloromyotomy
44	Pyloric stenosis	4	8	Pyloromyotomy
45	Pyloric stenosis	4	9	Pyloromyotomy
46	Pyloric stenosis	4	10	Pyloromyotomy
47	Pyloric stenosis	4	10	Pyloromyotomy
48	Pyloric stenosis	4	10	Pyloromyotomy
49	Pyloric stenosis	4	12	Pyloromyotomy
50	Pyloric stenosis	4	12	Pyloromyotomy
51	Pyloric stenosis	4	12	Pyloromyotomy
52	Pyloric stenosis	4	13	Pyloromyotomy
53	Pyloric stenosis	4	13	Pyloromyotomy
54	Pyloric stenosis	4	14	Pyloromyotomy
55	Pyloric stenosis	4	14	Pyloromyotomy
56	Pyloric stenosis	4	14	Pyloromyotomy
57	Pyloric stenosis	4	14	Pyloromyotomy
58	Pyloric stenosis	4	14	Pyloromyotomy
59	Pyloric stenosis	5	0	Pyloromyotomy
60	Duodenal stenosis	3	3	Duodenojejunostomy
61	Duodenal stenosis	4	5	Duodenojejunostomy
62	Duodenal stenosis	4	10	Duodenojejunostomy
63	Duodenal stenosis	4	15	Duodenojejunostomy
64	Jejunal stenosis	4	13	Jejunojejunostomy
65	Ileal stenosis	4	15	Ileoileostomy
66	Annular pancreas	3	6	Duodenojejunostomy
67	Annular pancreas	3	7	Duodenojejunostomy
68	Annular pancreas	3	12	Duodenojejunostomy
69	Annular pancreas	4	0	Duodenojejunostomy
70	Annular pancreas	4	7	Duodenojejunostomy
71	Annular pancreas	5	0	Duodenojejunostomy
72	Malrotation	4	8	Ladd's operation
73	Obstruction from jejunal bands	4	12	Release of bands
74	? Obstruction	2	8	Abdominal exploration
75	? Obstruction	4	11	Abdominal exploration
76	? Obstruction	4	13	Abdominal exploration
77	Intussusception	4	9	Reduction
78	Omphalocele	3	6	Repair
79	Omphalocele	4	0	Repair
80	Omphalocele	4	4	Repair
81	Omphalocele	4	12	Repair
82	Omphalocele	5	0	Repair
83	Diaphragmatic hernia	4	13	Repair
84	Strangulated inguinal hernia	4	0	Repair
85	Strangulated inguinal hernia	4	4	Repair
86	Sacrococcygeal teratoma	3	4	Removal of tumor
87	Sacrococcygeal teratoma	3	7	Removal of tumor

*Ten of these babies died subsequent to their hospital discharge. In some, the death was related to the original surgical condition; in others it was not.

†In newborn period, operations consisted of closure of tracheo-esophageal fistula, marsupialization of upper esophageal pouch in neck, and gastrostomy. These children were rehospitalized at subsequent times for intrathoracic or extrathoracic reconstruction of the esophagus.

‡Repair of anus deferred for subsequent hospital admission.

procaine infiltration 59 times, ether 27 times, and avertin plus local in 1 instance. (To show the recent trend in preference of anesthesia, of the 19 cases treated in 1951, all except one—local—received cyclopropane.)

Of the 87 infants who were discharged from the hospital well, 10 have subsequently died because of conditions either related or unrelated to their original disease. In addition, it is known that 4 are mongoloids, one is mentally retarded, and another has retrolental fibroplasia of the eyes. Thus, out of the 87 who were originally discharged from the hospital, 71 are sound in mind and body.

CONCLUSIONS AND SUMMARY

One hundred and fifty-nine premature infants requiring surgery have been treated during the past 16 years. The various conditions requiring surgery included a very wide variety of malformations and conditions peculiar to early life. In more than a quarter of the infants, multiple anomalies were present.

Despite the small size and the critical condition of many of these infants and the extensiveness of their operative procedures, only 1 death occurred on the operating table. Eighty-seven patients were discharged from the hospital, a survival rate of 54 per cent. Of the survivors, 16 are known to have died subsequently or to have serious defects of various sorts, leaving 71 subjects who have had their abnormality corrected, have ultimately survived, and now possess good health and development.

Certain physiological limitations are imposed upon the newborn infant by prematurity. Based upon an understanding of these limitations and as a result of the experience gained in the surgical treatment of a large number of premature infants, certain principles of therapy have been formulated which are summarized herewith.

REFERENCES

1. Denton, R., and Smith, R. M. Portable humidifying unit—II, large capacity metal nebulizer. Am. J. Dis. Child., 1951, 82: 433.
2. Levine, S. Z., Gordon, H. H., and Marples, E. A defect in the metabolism of tyrosine and phenylalanine in premature infants—II, spontaneous occurrence and eradication by vitamin C. J. Clin. Invest., 1941, 20: 209.
3. Smith, C. A. The Physiology of the Newborn Infant. 2nd ed. Springfield, Ill.: Charles C Thomas, 1951.

EDITORIALS

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HORIZONS IN BURN SURGERY

WAR, pestilence, and catastrophe create a multitude of new problems for the surgeon as well as augment the ever-present problems of acute traumatic care. The bomber, tank, and flame thrower greatly multiply the numbers of potential burn victims, but even these diminish in importance when considering complexities to be encountered in dealing with the victims of atomic bomb explosions. As a matter of fact, no other event has so aroused interest in thermal burns.

In order to accomplish better and more efficient treatment of the burned patient, there are specific problems hovering over the horizon of burn surgery which must have solution.

In the past 10 years, modest advances have been made in the better understanding of some of the mechanisms responsible for burn shock, but many gaps remain. Most surgeons realize salt is required to combat some of the features of burn shock but the salient question remains —how much salt and water are needed? Oral saline is quite effective in the less severely burned patient. The ease of administration suggests its advantage in the treatment of mass burn casualties; however, how effective this therapy is in the treatment of the more severely burned patient has not as yet been established.

Certain plasma substitutes for instance, polyvinyl pyrrolidone (periston), still require serious study in the severely burned patient. The clinical problem of whole blood requirement for severe burns must be further explored; such studies should employ available methods for tagging of the red blood cell in order to determine accurate red cell mass in the burn patient.

The enthusiastic use of ACTH in the early treatment of the burn patient has not been substantiated. The stress response in the burned patient has been demonstrated to be so intense that it is unlikely it could be further augmented by the administration of ACTH. ACTH therapy may be found useful in later phases of burn care. The value of cortisone in the early days post burn has not as yet been delineated. Cortisone in amounts up to 300 milligrams per day has been given to some severely burned patients with no dramatic improvement. Real advances in this field await the development of simple and more precise methods for the identification of small amounts of adrenal steroid compounds in both blood and urine. This requires the support of fundamental biochemical research in clinical endocrinology. Such studies should provide an opportunity to answer the question, "Just what is the adrenal response?" qualitatively and quantitatively in severe burns.

Would the burn patient benefit by therapy designed to abate the stress response rather than augment it? The suggestion of Selye of counteracting ACTH effects with the somatotrophic (growth) hormone of the pituitary compels serious consideration. Such studies may lead to methods for altering the early catabolic response, the course of invasive wound infections, and harmful fluid and salt transfers in the severely burned patient. Because many growth hormone preparations contain thyreotrophic hormone the action of this principle in altering the stress response should be discerned.

The clinician is still confronted by the badly burned patient who develops severe liver dysfunction. When the use of tannic acid was abandoned in burn therapy it was hoped that liver dysfunction would not occur. In the severe burn, liver dysfunction is still seen almost as often now as during the heyday of tannic acid therapy. Liver failure appears to be responsible for some of the early deaths in burns. The problem may be one of prevention of liver dysfunction rather than treatment. The hormonal imbalance following severe burns should be studied in relation to this liver damage, with particular attention to the many enzyme systems of this organ.

With the improvement of shock therapy in burns, renal failure is seen much less commonly than 10 years ago, but yet so frequently as to warrant further investigation. It often follows a lapse of several hours between the time of injury and the beginning of shock therapy in the elderly patient. Studies should include more general therapeutic trials of the artificial kidney or similar methods of blood clearance.

In recent years, there has been little discussion of toxins in burn shock. There is a real need for knowledge of the role of bacterial metabolites as toxins in severe burns. Present clinical efforts to prevent toxin absorption include the early surgical excision of the burn slough. If this procedure should prove valuable, there would be a real need for skin banks for temporary wound coverage. Studies on burn toxins should be combined with those on renal and liver dysfunction in the severely burned.

There is no single ideal method for burn wound care. Surgeons are learning the advantages and limitations of both the closed and open methods. The apparent ease of handling large numbers of burn casualties by the open method suggests that careful study should be made to learn its true limitations. Improved adaptations of the closed method for burned fingers and hands are needed with accent upon simple but effective splinting of the hands. Ordinary surgical gauze adheres to the granulating burn wound unless it is covered with some ointment or oily substance. If the dry wound principle is to be employed for all stages of local burn care, study should be pursued to develop a more universal applicable nonadherent dressing.

In spite of available potent antibiotics of the broad spectrum type, chronic infection of the burn wound of long-standing is all too frequent. Cross-infection of burn wounds is more often the rule than the exception when large numbers of burned patients are involved. Indeed, in most surgical clinics visited recently, burn wound infection appears just as frequently as it did 10 years ago. Some groups should evaluate without bias the feasibility of using Colebrook's layout for a burn center. Colebrook's plan may appear too complicated for general adoption, but the problem of a severe burn wound infection and cross-infection will be with us until some equally effective plan is adopted. Our experience would indicate that dressing all burn wounds in a central dressing station, without some such

control as Colebrook's, may result in more serious cross-infection than when these individuals are dressed on the open wards. Continuous effort must be made to develop and employ a closed dressing which cannot be "soaked through."

Investigations of the frequency of development of insensitivity to antibiotics in organisms responsible for burn wound infection should be pursued vigorously with special attention to pyocyaneus and proteus strains.

The excision or enzymatic débridement of the burn wound allows early closure of the deep burn by skin graft. Streptokinase-streptodornase, and proteinases from clostridial cultures, trypsin, and other enzymes require clinical trial to answer such questions as: (1) Are these preparations effective? (2) When is it clinically useful to employ them? (3) In how large a wound is their use safe? (4) Do they damage adjacent wound skin? (5) Are they useful as preparation for surgical débridement?

Because of the likelihood that more and more extensively burned patients may survive the shock period and therefore require wound débridement and grafting, it is hoped that efforts to preserve the life of homografts will be made. The failure of cortisone and ACTH to prevent the dissolution of such grafts should turn such efforts in the direction of the fundamental aspects of the homograft problem.

There is a tendency in some experimental burn research to ignore the fact that the clinical subject with burns may have additional severe complicating trauma. For this reason, studies of the effect of concommitant injury to burning such as fractures, radiation, and cranial and chest injuries must also be made in preparation for any sort of mass casualties, especially those of atomic attacks.

On the horizon of the problems in burn patients loom many questions such as better nutrition, the many faceted problem of rehabilitation, and the teaching of the medical students and training of resident surgeons and nurses in what is already known about modern methods of burn care. The importance of teaching certain fundamental principles of physiology, chemistry, and bacteriology to the young surgeon is well recognized. The severely burned patient presenting a problem in each of these fundamentals is the ideal study case for the surgeon in training. This is of the utmost importance to the medical department of the Armed Forces on whom, in the event of global war, must necessarily fall much of the responsibility for the care of all wounded.

EVERETT IDRIS EVANS.

THE HEPATIC ARTERY

EVERY properly planned scientific research has a rainbow round the corner. It is this which attracts thousands of investigators who, years ago, would have pushed off for unknown lands. The possibility of an unexpected development which would make a pattern out of disorder, which would glamorize a drab array of facts, is the chief appeal of scientific research. We submit the recent knowledge of the hepatic artery as a case in point; that the knowledge is useful, is all to the good.

Surgeons doing a cholecystectomy are careful not to injure the hepatic artery, for its ligation results in death in about 75 per cent of cases. This accident may be contrasted with the relative harmlessness of diverting the blood from the portal vein into the inferior vena cava, an operation that has been deliberately undertaken for the relief of portal hypertension. Although four fifths of the blood supply to the liver is supplied by the portal vein and only one fifth by the hepatic artery, nevertheless the former fact did not appear surpris-

ing, it being the belief that the artery had an essential function to perform in nourishing this large organ, possibly because the blood in it was delivered at high pressure and was fully oxygenated.

In experiments extending over a period of nearly 20 years, Markowitz and his colleagues investigated this peculiar dual blood supply of the liver. They found as had many others before that when the hepatic artery in dogs is ligated beyond its last tributary, death results almost invariably within 24 to 48 hours, and at autopsy the liver has been transformed into a large stinking, mushy organ, which microscopically shows almost total disorganization, the liver structure containing millions of anaerobic rods resembling the Welch bacillus. On the other hand diversion of the portal vein from the liver results in minimal fibrosis with but little alteration in function of the liver or the health and longevity of the animal. The attempt was first made to arterialize the portal blood stream, as by anastomosis of the splenic artery to the splenic vein, or by joining the renal artery to the splenic vein. Markowitz and associates hoped that by this means they could safely ligate the hepatic artery without the development of the characteristic necrosis of the liver. These experiments were unsuccessful because thrombosis occurred at the anastomotic site between the artery and the vein. It would appear that, in the dog, a procedure which is successful for joining an artery to a vein in the groin or in the neck is not successful when performed in the abdomen; possibly this is because of the mobility of the part or because of the small size of the vessels. Accordingly, about 4 years ago the splenic artery was anastomosed to the splenic vein by Markowitz, Rappaport, and Scott, using transflex tubing which had been previously siliconed. The animal was given penicillin to protect any break in aseptic technique. The hepatic artery was then effectively ligated and the experimenters watched the animal with great interest. It was alive and well 2 days later. Under ether anesthesia the animal was explored to see if blood was flowing through the tubing; it was found to be firmly clotted. The liver appeared normal. When this experiment was repeated it gave the same results. A series of experiments was then undertaken in which the hepatic artery of dogs was ligated, and the animals were given penicillin daily to see if they would survive. The totally unexpected observation was made that a few doses of penicillin could replace the function of the hepatic artery indefinitely with only minimal changes in the liver. The gallbladder, of course, atrophies. About 35 per cent of the dogs subjected to this operation die, but half of these fatalities are due to bile peritonitis from rupture of the gallbladder, a rupture that is inevitable in some instances because of gangrene of the gallbladder.

The hepatic artery has thus a unique function, one not possessed by any other artery in the body. The liver is supplied by a large volume of venous blood and, in the case of dogs, almost constantly harbors anaerobes. It is the function of the hepatic artery to discourage the proliferation of such anaerobes when there are focal areas of necrosis, which, as is well known, permit the germination of anaerobic spores. Whether such anaerobes regularly exist in *human* liver tissue is not easily settled by needle biopsies, since in order to demonstrate anaerobes in the *dog's* liver, it is necessary to incubate large slabs of liver anaerobically, the dead liver itself being the best culture medium. Needle biopsies or swab cultures of dog liver only occasionally give positive growth, whereas when treated according to the original technique of Wolbach and Saiki, the incubated liver almost regularly becomes transformed into an organ resembling closely what

is seen following ligation of the hepatic artery in the living animal. However, it is logical to suppose that the liver, situated at the head of the portal vein which drains a cesspool, is constantly embolized by bacteria from the bowel. Once the anaerobes proliferate and get a head start, their toxin causes massive necrosis of the organ, comparable to gas gangrene in a wounded soldier.

The idea that bacteria proliferate in the anoxemic liver, whatever the cause of the anaerobiosis, would be a reasonable speculation as a result of these experiments. Fine and his associates, of Boston, have since shown that death in otherwise irreversible hemorrhagic shock in dogs could largely be prevented by giving the animals large doses of aureomycin, whereas dogs similarly treated but without aureomycin died in 90 per cent of cases. The administration of antibiotics in all cases of shock is thus logical. Already surgeons have undertaken the treatment of advanced hepatic cirrhosis by ligation of the hepatic artery under the protection of antibiotics. William F. Rienhoff Jr. of Baltimore and Jacob K. Berman of Indianapolis each report successful cases of decompression of the portal vein by ligation of the hepatic artery. There undoubtedly will be further applications of this knowledge. For example, carcinoma at the head of the pancreas can now be more radically treated in some instances in which the hepatic artery is involved in the growth. It is possible that secondary carcinoma of the liver may be treated by ligation of the hepatic artery. Segall almost 30 years ago showed that hepatic metastases obtained almost all their blood supply from the hepatic artery and none from the portal vein.

Possibly the chief value of these experiments may turn out to be in medical diseases of the liver in which anoxia and necrosis of greater or lesser parts are common, for example, total necrosis of the liver (acute yellow atrophy) and infectious hepatitis.

This research is strictly the product of time. Without penicillin it could never have been established whether, after tying the hepatic artery, the bacteria caused the massive necrosis, or were secondary invaders of a rich culture medium of ischemically vulnerable tissue. Needless to say, without the work of Mann, Dragstedt, Ellis, Mason, and other preceding investigators, the finding might have been overlooked. The pattern constructed by them needed one missing piece which was easily recognized when it turned up.

JACOB MARKOWITZ.

THE SURGEON'S LIBRARY

THE BOOK SHELF

THE SOUR GRAPES OF VALMY

RUDOLPH MARX, M.D., F.A.C.S., Los Angeles, California

SEPTEMBER 20, 1792, was the day of decision for the French Revolution. On this day the National Convention met at Paris for a final vote on abolishing the monarchy and proclaiming a republic. At the same hour, 120 miles to the east, a battle was being fought which was to determine the fate of the Revolution and the course of European civilization.

The citizen-soldiers of France were defending the road to Paris against the mercenaries of Prussia and Austria. They were holding a flanking position on the plateau of Valmy on the eastern edge of the undulating plains of the Champagne—a region designed by topography to serve as one of the natural battlefields of Europe.

At the misty dawn of September 20, 1792, the odds of the French Army against the Prussian-Austrian troops seemed poor indeed. It was obvious that the tenets of the Revolution—liberty, fraternity, egality—were hardly compatible with the principles of an army—subordination and discipline.

The nucleus of the French Army still consisted of veterans of the old régime. But their efficiency had been impaired by a dearth of commissioned officers, most of whom had been members of the nobility. Raw levies and unruly volunteers made up the replacements.

Barely 4 weeks before the decisive encounter, the trusted commander-in-chief of the Army of the Center, the Marquis de Lafayette, had been forced to flee for his life, suspected of anti-Revolutionary activities. He had been supplanted by an unknown general, Charles du Dumouriez. The corps which bore the brunt of the battle was commanded by Francois de Kellerman, also a newcomer.

Arrayed against the motley army of the Revolution, led by unproved generals, was the cream of the Prussian Army, supported by Austrian cavalry. Superior in numbers and discipline, trained in the tradition of Frederic the Great, they were led by a celebrated general, the Duke of Brunswick, and accompanied by the King of Prussia in person.

During several previous encounters the invading army had brushed aside the French and in short order taken the fortresses of Longwy and Verdun. With unexpected ease they had forced the passes of the wooded hills of the Argonne, the last natural barrier on the road to Paris.

On the day preceding the battle the Allies were marching down through the vineyards of the Champagne, confident of an early conclusion to a leisurely promenade into Paris. They were taken by surprise with the intelligence that the Revolutionary forces had halted their retreat and were concentrating on the left flank of the Allies. The Prussian command reacted promptly, changed the direction of march, and deployed in battle formation opposite the French.

On the gray morning of the 20th of September, 1792, the French were poised on a low ridge between St. Menehould and Valmy. The Prussians were massed on a chain of hills across a narrow valley, flanked by Austrian cavalry. As the fog lifted the Prussian artillery began a heavy cannonade of the French position. This was soon answered by veteran French gunners. Early in the afternoon the Prussian infantry advanced in massed formation. The raw levies in the French ranks wavered as the row of glittering bayonets moved toward them at a slow and seemingly relentless pace. Rallied by General Kellerman, they held, and opened fire.

The advancing juggernaut hesitated and came to a halt at the foot of the hill; then slowly it retreated to its old position. Incredulous at the poor showing of his famous infantry against the "contemptible Parisian rabble," the king let

Fig. 1. The Battle of Valmy (from a painting by Horace Vernet reproduced from *Histoire de France*, Library Larousse, vol. 2, p. 234).

loose a tirade and led them in person to a second attack. But on this day even the king could not arouse his guards from their strange lethargy. After a short advance with moderate casualties, they staggered back for a second time.

The astonished French did not follow up their advantage. The Allied Army lingered on in the vicinity for some 10 days after the battle, and then retreated to the Rhine without firing another shot.

Attached to the staff of the Duke of Brunswick as an unofficial observer was the poet, Goethe, who later published a war diary under the title, "Campaign in France in 1792." Goethe describes the scene of consternation and dejection among his companions which he witnessed on the night after the battle. The officers of the staff were sitting about in a circle in a cold bivouac, afraid to light a campfire. "Most of them were silent," the poet wrote. "And in fact the power of reflection and judgment was wanting to all. . . . At last I was called upon to say what I thought of the engagement. This time I said, 'From this place and from this day forth commences a new era in the world's history, and you can all say that you were present at its birth.' "

History has shown that Goethe was correct in his poetical divination. The "Cannonade of Valmy," as the encounter was later derisively called, proved in fact to have been a decisive battle of the world. It was the first test in which the citizen soldiers of France stood up and prevailed against the mercenaries of the old European order, saving the French Republic at its birth. This victory gave the Revolutionary army the confidence and the time needed to become welded into a new dynamic force. Led by inspired young generals and imbued with the ideals of the Revolution, it became the instrument which carried the tricolor and the message of the rights of man over Europe.

Up to recent times the riddle of the upset at Valmy had not been satisfactorily solved. Students of military history could not understand why the renowned, well disciplined Prussian infantry had failed so ignominiously at Valmy after suffering only comparatively slight losses—fighting under the same colors which their fathers had carried to victory over heaps of corpses at the bloody battles of Prague and Torgau. Neither could it be comprehended why an experienced general like the Duke of Brunswick gave up the campaign so readily without making any further attempt to dislodge the French.

With a degree of justification, Goethe and some of his contemporaries blamed the failure of the campaign on the unseasonable rains that had preceded the battle. Foxy armchair strategists hinted that the Duke of Brunswick did not really wish to crush his brother in arms, General du Dumouriez, who after all had been an officer of the old régime and who actually deserted to the Austrians in the year following Valmy.

Earlier historians overlooked or ignored the greatest of all forces to decide the battles of the past—the most drab and the least glamorous of the Four Horsemen—disease. Not superior valor or better generalship defeated the Prussians on the hills of Valmy. An invisible ally came to the aid of the French Army on the day of the battle and carried the Revolution to victory—the red dysentery.

During the weeks preceding the battle, continuous summer rains had transformed the roads into

rivers of sticky mud, retarding the Allies' advance and impeding the flow of supplies. The Allied soldiers were hungry and cold during that September. Not only were food and shelter scarce in the thinly populated Argonne; only a few springs of good water were to be found. The troops had to use water from polluted wells and ditches. On the day before the battle the soldiers passed through the hills of the Champagne between rows of vines heavy with grapes. The half-famished men gorged themselves with the grapes, still green and sour from lack of sunshine. In consequence, on the day of the battle there occurred a violent flare-up of an epidemic of dysentery which had been smoldering among the ranks.

It was this unseen enemy that decimated, debilitated, and discouraged the Prussian infantry, slowing down their attack, so that they were easily repulsed by the unexpected stand of the opponent. The ravages of the same epidemic made it impossible for them to resume the offensive and forced them to retreat from their strategically unfavorable position. Even in flight they could not shake off the invisible foe. Less than two-thirds of the original number returned to Germany.

REFERENCES

1. Creasy, Sir Edward S. and Murray, Robert H. Decisive Battles of the World. Harrisburg, Pa.: The Military Service Publishing Co., 1943.
2. Goethe. Campaign in France in 1792. Collected Works.
3. Zinsser, Hans. Rats, Lice and History. New York: Blue Ribbon Books, 1938.

REVIEWS OF NEW BOOKS

NO one can read the volumes *Post-Graduate Lectures on Orthopedic Diagnosis and Indications*[1] by the dean of American orthopedic surgeons without being impressed by the wide range of problems covered by the author's simple and direct approach and by his very serious and sincere effort to assess the results obtained in the treatment of many diverse and difficult conditions.

Lectures I to IV of Volume 2 are devoted to anterior poliomyelitis. Lecture II on the clinical pathology contains an exceedingly clear-cut picture of the acute phase and clinical types of the disease and a discussion of the symptoms and diagnosis that reflects the author's wide personal experience. In Lecture III on conservative treatment he gives generous credit to other workers. Concerning the controversial subject of the Kenny method he says (p. 30) ". . . in one respect at least the method deserves a great deal of credit. It has helped to break a tradition of absolute and prolonged immobilization, which in some quarters had been greatly abused, and which not only disregards established physiological facts, but is also contrary to the old teaching of Lovett. He was a strong advocate of the application of heat and of muscle re-education. So far as the muscle educational part of Kenny's system is concerned, it is an excellent and refined method of dissociating substitutionary mass movements by individual muscle training and selective muscle exercises . . . the fact that others have emphasized the application of heat and the practice of muscle training (Morquio) before should, we believe, not detract from the Kenny method insofar as it represents a definite technical advance."

In Lecture IV on operative treatment he covers the entire field of shoulder, elbow, wrist involvement, thenar palsy, and disabilities of the lower extremities. As in his other writings the author attempts to evaluate in percentage tabulation the results of the procedures carried out and the reader is left with a definite picture of what can be accomplished in these difficult and trying conditions.

In Lectures V and VI on paralytic scoliosis and spastic paralysis, as in the discussion of treatment of the sequlae of poliomyelitis, the author emphasizes the difficulties involved in surgical corrections and the guarded prognosis that must be given. One simple statement "Sympathectomy is hardly ever applied today for the relief of spastic paralysis" (p. 71) cannot fail to call to mind how enthusiastically this procedure was accepted at one time as a corrective treatment for many types of spastic conditions and how disappointing were the results.

Section B on static disabilities includes 4 lectures on lumbosacralgia or low back pain, on idiopathic scoliosis, on internal derangement of the knee, and on static deformities of the foot and ankle. In the different diagnosis of that common and often baffling condition—low back pain—the author's clear cut discussion of the pathogenesis and his differentiation of the various pain patterns has done much to bring order and exactness in the understanding and treatment of this troublesome condition.

The discussions on internal derangement of the knee joint and static deformities of the foot and ankle concern chiefly the surgical treatment and its results. The subject of conservative treatment of flat foot is limited to 2 pages, and one regrets the lack of illustrations to help clarify the suggested plan of treatment.

In Volume 3 Steindler presents in 12 well organized lectures the important subjects of tuberculosis of the skeletal system and osteomyelitis. These lectures are well documented with numerous excellent illustrations of patients, of pathological specimens and of roentgenograms. Some of the material presented has become of historical rather than of current surgical interest and the author would probably be the first to agree that the time will soon come when the entire subject of bone and joint infection, both tuberculous and nontuberculous, will have to be reviewed in the light of the changes in treatment that have resulted from the use of streptomycin, penicillin, and other effective antibiotics.

SUMNER L. KOCH.

IN the small volume of 325 pages entitled *Atlas of Genito-Urinary Surgery*[2] standard operative procedures are briefly but clearly presented. The successive steps of the various operations are shown in a series of beautiful line drawings by Charles Stern. The accompanying text is brief and to the point. The entire volume is printed upon a glossy paper of superior quality. Both type and illustrations are of such sharpness and size that they can be observed at a glance. This makes for very easy and pleasant reading.

In spite of the general excellence of this volume the reviewer feels that a few criticisms are in order. The failure to employ an extramucosal suture technique and the exposure of knots to the lumen of the urinary tract is not in keeping with the refined techniques of modern urologic surgery. The leaving of clamps *in situ* as described in the section on intracapsular nephrectomy is also unnecessary and inexcusable today. The chapter on transurethral resection is too

[1] POST-GRADUATE LECTURES ON ORTHOPEDIC DIAGNOSIS AND INDICATIONS. Vol. 2. PARALYTIC DISABILITIES AND STATIC DISABILITIES. Vol. 3. TUBERCULOSIS OF THE SKELETAL SYSTEM AND OSTEOMYELITIS. By Arthur Steindler, M.D., F.A.C.S. Springfield, Ill.: Charles C Thomas, 1951, 1952.

[2] ATLAS OF GENITO-URINARY SURGERY. By Philip R. Roen, M.D., F.A.C.S. New York: Appleton-Century-Crofts, Inc., 1951.

sketchy to be of value and describing such a highly specialized technique might better have been omitted.

In spite of these minor criticisms this atlas is to be highly recommended as a reference book for interns and residents. The experienced urological operator as well will enjoy reading this excellent little volume.

FREDERICK A. LLOYD.

The well written and beautifully illustrated fourth edition of Watson-Jones' *Fractures and Joint Injuries*[1] is a great credit both to the author and the publishers.

Probably no better review could be written than that which the author has presented in his preface:

"Every page has been corrected or rewritten, new chapters have been added, and several hundred new illustrations have been prepared. There are new chapters on wound-shock and the adaptation syndrome in its relation to shock; on the treatment of open fractures and joint wounds, chemotherapeutic control of infection, early closure of wounds by secondary suture or skin grafting, and plastic surgery in fracture treatment; on transplantation of bone, cancellous bone grafting and intramedullary nailing with a series of case reports of typical bone-grafting operations; and on fatigue fractures and pathological fractures, with a review of bone disease that covers almost the whole of orthopaedic surgery."

"A chapter is included on the reactions of bone to metal . . . A vigorous attack is made upon the almost universally accepted belief that contact-compression, lag screws, slotted-plates, compression-clamps, and early weight-bearing promote the union of fractures. . . . Forcible compression of bone is pathological rather than physiological, and it avails in the treatment of fractures only in so far as it promotes immobility and protects from shear. Believing this, and denying the view that is held so widely, I reiterate that plates and screws do not hold fragments apart; they scarcely hold them at all—certainly not for more than a few days or weeks. It is indeed unwarranted faith in the capacity of screws to provide fixation of bone that is the cause of nonunion of plated fractures. . . . We should dismiss the phrase, 'internal fixation of bone'—there is no such thing; and there is only internal suture, some sutures being more efficient than others. I still believe firmly that, apart from interposition of muscle and periosteum, the sole important cause of nonunion is inadequate immobilisation."

Throughout the volume the author's ideas are illustrated and fortified with a wealth of excellent illustrations, many of them in color, that are convincing and so well placed in relation to the text that reading it becomes a pleasurable experience.

From such a wealth of important and well presented material it is difficult to single out individual chapters or subjects for special mention.

Chapter 3 on "Adhesions and Joint Stiffness," and Chapter 8 on "Clinical and Radiographic Diagnosis," contain so many wise observations based on wide experience that one feels they should be required study for every young surgeon who cares for patients with bone and joint injuries. Chapters 10 and 11, "Operative Reduction of Fractures" and "Reactions of Bone to Metal" should be "must reading" for the surgeon embarking upon open treatment of fractured bones.

Chapter 13, "Open Fractures and Joint Wounds," is a profusely illustrated discussion of the problem, with illustrations of some almost inconceivably severe injuries followed by remarkable recovery and return of function. Many of the cases described constitute outstanding tributes to the achievements of the author and his co-workers during World War II.

Chapter 14 on "Transplantation of Bone," and Chapter 17 on "Pathological Fractures," assemble in 40 pages and 80 pages a wealth of valuable material, gathered from many sources and again fortified with many excellent illustrations. In fact, Chapter 14 consists largely of case records chosen to illustrate the principles laid down, principles which are emphasized in the descriptive legends and demonstrated by numerous illustrations, many of them full page, and all exceedingly well reproduced.

Throughout this volume are many observations which one would like to quote at length, and which could well be placed in black-faced type in every text book of surgery. To mention only a few:

On joint injuries (p. 45), "if the injured joint is treated by early movements, and the torn tissues are not protected there is *repeated* exudation; and it is the soaking of tissues with fibrinous serum day after day that causes dense adhesions. The practice of treating dislocations and fractures of the shoulder by immediate movement defeats its own object; instead of preventing stiffness it aggravates stiffness. The correct treatment is to protect and support the torn tissues until they are healed, to continue exercises of the distal joints, and to begin active but not passive movements of the injured joint after 2 or 3 weeks."

Concerning tourniquets (pp. 121–122), "More limbs have been lost by the use of tourniquets than have been saved"; and, "There is greater danger in the upper limb than in the lower limb, but in neither upper nor lower limb is there complete safety except with the controlled pressure of a pneumatic tourniquet. The partly skilled first-aid worker who has been taught to improvise tourniquets from bandage or cord, tightened with pieces of wood, is a most dangerous person. There is danger in applying the tourniquet too tightly; there is danger in not applying it tightly enough; there is danger of killing the patient by the renal complications of tourniquet pressure; the only danger that is remote is that the patient will bleed to death for lack of a tourniquet. . . Abolish tourniquets from first-aid equipment!"

Concerning antiseptics and chemotherapy, (p. 239 and p. 246), "Sir Alexander Fleming, discoverer of penicillin, said: 'The greatest of all antiseptics is liv-

[1] FRACTURES AND JOINT INJURIES. By Sir Reginald Watson-Jones, B.Sc., M.Ch. Orth., F.R.C.S., F.R.A.C.S. (Hon.), F.A.C.S. (Hon.). Vol. 1, 4th ed. Baltimore: The Williams & Wilkins Co., 1952.

ing tissue.' Carbolic acid and other powerful antiseptics are useless because they can destroy only bacteria that lie on the surface and, moreover, they also destroy cellular tissues. It is upon the vitality of tissues that the real defence against infection depends. . . . there can be no support for the view that when chemotherapy is available the operation of wound excision is no longer urgent and that it can be performed at leisure. No antibiotic can reach the depths of a mass of dead muscle that has no circulation; the action of sulphonamides is inhibited by dead material and by pus fluid; and many bacteria are not sensitive to penicillin. Chemotherapy is a most valuable adjunctive treatment, but it cannot take the place of wound excision and it cannot alter the principles upon which that operation is based."

Concerning the use of foreign material in open fractures (p. 245), "Since one of the main purposes of operation is the removal of foreign bodies, there can be no justification for burying other foreign bodies such as wire, screws, or plates. Even sterile catgut is a foreign body which causes sero-fibrinous exudation and increases the danger of infection, and the less catgut that is buried the better."

Concerning the "scraping" of sinuses (p. 276), "Sequestrectomy is not a 'scraping operation' . . . a curette or spoon is not needed; a gouge or chisel should seldom be used. Ideally, the only instruments required are a scalpel and a pair of forceps. If every sequestrum or foreign body can be exposed by soft-part dissection and lifted out without chiselling of bone the wound will heal by first intention."

One could go on at length but enough has been said to emphasize the fact that this volume is a splendid, a comprehensive, and most desirable contribution to the subject of bone and joint surgery and that it deserves high praise from every standpoint.

SUMNER L. KOCH.

A systematic survey of the physical and biological bases of radiation therapy is presented in *Grundlagen der Strahlentherapie; Physik, Biologie und allgemeine Therapie*[1] by Dr. Kepp. The first part is devoted to radiation physics, the second to radiobiology and general aspects of radiotherapy of malignant neoplasms. The physical section presents a classical discussion of the nature, production, and physical properties of x-rays as well as their interaction with matter, dose measurement, and distribution. Also included is a discussion of natural and artificial radioactivity as well as corpuscular radiation (cathode rays, proton, deuteron, and neutron radiation).

The biological section, beginning with the primary processes of radiation biological action and the influence of wave length and chronological and spatial distribution of radiation, proceeds to a discussion of radiation effect on cells, tissues, and specific organs. Genetic and systemic radiation effects as well as some aspects of radiation protection are discussed. The part devoted to radiation treatment of malignant tumors deals with general considerations such as variations in radiosensitivity, tumor dose and its distribution in time and space, radiation quality, and comments on general indications for irradiation. Reports in the literature as recent as 1950 have been included, thereby bringing both the physical and biological sections up to date.

It is of interest that the author is professor of obstetrics and gynecology at the University of Gottingen. This book can serve admirably as an introduction to the subject for both physicians and students.

ISADORE LAMPE.

A most attractive volume whose stated purpose is "to bring together recent work in the gastroenterological aspects of medicine and surgery" is entitled *Modern Trends in Gastro-Enterology*[2] edited by F. Avery Jones. This combining of discussions germane to both medicine and surgery into one volume is evidence of the recently increasing tendency toward combined medical and surgical study and treatment groups; the breadth of view engendered by this approach is highly desirable and it is gratifying to see the principle extended to the publishing field.

There are 34 chapters, no 2 of which are written by the same author, there being a total of 45 contributors. Subjects range from "Anaemias of the Alimentary Tract," "Relationship between the Alimentary Tract and the Cardiovascular System in Disease," "A Psychiatric Approach to Digestive Disorder," "Abdominal Pain," through various diseases of the salivary glands, esophagus, stomach, intestine and colon, to conclude with discussions of jaundice, liver disease, portal hypertension, and pancreatic lesions. All of the authors are English, hence the book reflects British opinion for the most part; however, the majority of the chapters gain breadth of viewpoint through reference to work on both sides of the Atlantic. Multiple authorship usually brings about some disparity between manner of approach and style of writing, as is the case in this volume, but there is much valuable information in every chapter. While some of the articles are rather brief "textbook" types of discussion with reference to the literature, the vast majority are concerned either with the results of original research or with broad reviews of recent investigations.

Space does not permit of a detailed consideration of all the material presented. Somewhat over a quarter of the book is devoted to gastric physiology and pathology, including two valuable symposia, one on gastric secretion, the other devoted to peptic ulcer, its etiology, treatment, and complications. Chapter 13, "The Vascular Anatomy of the Stomach" by Bentley and Barlow, is a superbly illustrated

[1]GRUNDLAGEN DER STRAHLENTHERAPIE; PHYSIK, BIOLOGIE UND ALLGEMEINE THERAPIE. By Dr. Med. Richard Kurt Kepp. Stuttgart: Georg Thieme; New York: Grune & Stratton, Inc., 1952.

[2]MODERN TRENDS IN GASTRO-ENTEROLOGY. Edited by F. Avery Jones, M.D., F.R.C.P. New York: Paul B. Hoeber, Inc., 1952.

description of the blood vessels of the stomach wall, based upon the well-known research of these authors. "After Gastrectomy" by Capper is a most interesting compilation of various studies and opinions on physiological disturbances following gastric resection. The chapters on "Diaphragmatic Hernia," "Carcinoma of the Oesophagus," and "Carcinoma of the Stomach and Megacolon" are deserving of particular mention; all provide thorough consideration of recent work in these fields. Other particularly good contributions are the discussions of hepatitis and hepatic cirrhosis, and the final chapter on pancreatitis. The last contains an exhaustive review of the various etiologic elements, the course of the disease, and the various tests of pancreatic function as they relate to diagnosis and evaluation of treatment.

There is little need for adverse comment. Diseases of the salivary glands are considered in a manner resembling a textbook presentation, but the chapter does describe a wide variety of pathological conditions of these glands, however, briefly. The chapter on "Cardiospasm" stresses the element of spasm and treatment by dilatation; it is interesting that recent work on esophagitis is only briefly mentioned here, though considered in some detail in the excellent chapter on diaphragmatic hernia. Many surgeons, troubled by this difficult situation and the high recurrence rate following treatment, may feel that Mr. Wooler oversimplifies the problem when he states that 80 per cent of his patients were cured by hydrostatic dilation and "the remaining 20 per cent have had Heller's operation." It is disappointing to find a section on perforated ulcer with but one reference from this side of the Atlantic,—scant recognition of the many excellent publications on this subject by surgeons in both Canada and the United States. On the whole, however, there is little fault to find in a book of such a high general standard of excellence.

The volume is beautifully published and the illustrations are uniformly good though occasional reproductions of roentgenograms leave something to be desired. Both authors and publishers may well take pride in this attractive and informative volume which contains a wealth of information of great value to both internists and surgeons.

RUDOLF J. NOER.

THE proceedings of a conference which was sponsored by the Committee on Human Reproduction of the National Research Council has been edited by Earl T. Engle, M.D. of Columbia University. These proceedings are edited in book form which carries the title of *Studies on Testis and Ovary, Eggs and Sperm.*[1] The volume includes 14 separate articles related to the subject.

These reports are of great interest to gynecologists and urologists and to others who are interested in the problems of fertility and sterility. The chapters vary in content so that they are of value to both the clinician and research worker. One chapter stresses the absence of the vasa deferentia in quite a few men. Another provides evidence that defects of sperm which are due to radiation injuries are passed on to be seen two generations later. There is an excellent discussion on the semen quality in fertile marriage.

This book is easy to read and is recommended to those whose work is concerned with the problems suggested by the title. WILLIAM J. BAKER.

A brief and clearly stated up to date survey of information is contained in the volume on *The Rhesus Factor.*[2] The material is practical and is presented in a manner which makes this subject rather easily understood. The case reports presented illustrate well the practical application of rhesus factor testing in pregnancy, blood transfusions, and genetics. HUGH FLACK.

WHEN, in 1932, Sir Stewart Duke-Elder, already widely known as a prominent British ophthalmologist, issued the first volume of his *Text-Book of Ophthalmology*[3] the event was widely hailed throughout the world as of extreme importance. Over the intervening 20 years further volumes have appeared until now the fifth, and still not the final volume, has been published. The 5 volumes encompass nearly 6,000 pages and comprise the most complete source of accumulated information on the eye ever assembled in any language.

The present volume deals with the ocular adnexa and contains practically all that is known concerning the diseases and developmental anomalies of the eyelids, lacrimal apparatus, and orbit. Every condition is described in meticulous detail and in the language of one who is a master of expression. The overwhelming task of accumulating, editing, and preparing the final manuscript of a text of such monumental proportions is amazing. There has been a complete search of the literature of every condition described, and there are literally thousands of references to important ophthalmological papers published in every language. There is little wonder that Sir Stewart's textbook has become the standard reference work in ophthalmology throughout the entire world and that the appearance of each succeeding volume has been greeted as the major ophthalmic literary event of the year.

Because of the extreme completeness of this new volume, a characteristic of the previous volumes as

[1] STUDIES ON TESTIS AND OVARY, EGGS AND SPERM. Proceedings of a Conference Sponsored by the Committee on Human Reproduction, National Research Council, in behalf of the National Committee on Maternal Health, Inc. Edited by Earl T. Engle. Springfield, Ill.: Charles C Thomas, 1952.

[2] THE RHESUS FACTOR. By G. Fulton Roberts, M.A., M.D. (Cantab.). 3rd ed. London: William Heinemann, Medical Books, Ltd., 1952.

[3] TEXT-BOOK OF OPHTHALMOLOGY. THE OCULAR ADNEXA. Vol. 5. By Sir Stewart Duke-Elder, K.C.V.O., M.A., Ll.D., D.Sc. (St. And.), Ph.D. (London), M.D., F.R.C.S., Hon. D.Sc. (Northwestern), D. M. (Utrecht), F.R.C.S. (Edin.), F.A.C.S. St. Louis: The C. V. Mosby Co., 1952.

well, it is difficult to select any one part for special comment. The author's facile literary style, the excellent illustrations of which there are over 1,000, and the excellent printing job, all add to the value of the book.

Fortunate indeed is ophthalmology to have a disciple such as Duke-Elder, and no ophthalmological library can be built without his textbook as its cornerstone.

WILLIAM A. MANN.

IN the monograph *The History and Development of Neurological Surgery*,[1] Dr. Sachs has set forth a delightful, authoritative, and comprehensive account of all the elements which have combined in the formation of the specialty of neurological surgery from prehistoric times down to the present. Indeed, he has covered in large measure a good deal of the historical developments, not only of neurological surgery but of its allied subjects as well, namely, neurology, neuroanatomy, and neurophysiology, and has shown their relationship to the surgery of the nervous system as one discovery led to another during the various time periods.

The book is arranged in 6 chapters taking up the epochs in historical development from the Stone Age through the Egyptian, Greek, Roman, and Arabian periods, to the medieval and modern eras. In the last 2 chapters, those concerned with the beginning of present day neurological surgery and its latest developments, Dr. Sachs takes up the various conditions for which surgery of the nervous system is indicated and gives the details of the developments not only in the surgery of these conditions but in their diagnosis. It is in these chapters particularly that the author has made a most comprehensive and valuable correlation of the allied neurological sciences as they have affected neurological surgery, and the wealth of reference material which he has covered is most impressive.

In discussing the most modern phases of the subject in hand, Dr. Sachs has made several significant comments concerning his own views as to the efficacy of certain neurosurgical measures, and these are obviously of great value as coming from one who has been a leader and prolific contributor to the specialty from its earliest modern times.

The book is most attractively set up by the publisher, contains an excellent index and a comprehensive bibliography of 540 references. It will be welcomed as an extremely interesting and enjoyable narrative by all those who are concerned with neurological surgery and its allied sciences.

GILBERT HORRAX.

THE Year Book Publishers are to be congratulated on adding such a valuable book as *Surgery of the Chest*,[2] by Julian Johnson and Charles K. Kirby to their series of Handbooks on Operative Surgery.

This small volume lives up perfectly to its title. It gives with great clarity the essential steps in all of the accepted thoracic surgical procedures, and the illustrations which accompany each descriptive passage are so good that they constitute a veritable atlas of thoracic surgery. The accuracy and simplicity of the drawings are comparable with the authenticity of the text. Although this is a book on technique there is an excellent presentation of the basic physiology of the chest, and of the chief disturbances in physiology produced by various injuries and diseases. A brief consideration of the subjects of preoperative care, anesthesia, and postoperative management add appreciably to the value of the book.

If some point of disagreement could not be given it might suggest undue partiality, or inadequate study. The former could be true, but not the latter. Although no fault can be found with the book as a whole there are a few minor points that seem to warrant comment. The first has to do with anesthesia. In discussing the basic principles the need for adequate oxygenation of the blood is stressed, but no mention is made of the use of an intratracheal airway for this purpose. It is almost universal practice now to use intratracheal anesthesia and the authors probably take this for granted. However, as this book will be used by the uninitiated it seems worthwhile to mention this point. Another aspect of anesthesia has to do with its use in thoracoplasty, and other operations for tuberculosis, exclusive of pulmonary resections. Except when speed is of paramount importance, the use of local anesthesia has proven to be the most satisfactory in the hands of those who have done most of this work.

The only other point thought worth critical comment has to do with the description of drainage for empyema. Closed and open drainage are clearly described and illustrated, but the authors then obscure the fundamental difference between the two by showing how open drainage can be converted into the closed type. To most of the readers of this book this will not be confusing, but to the less experienced ones it probably will be so. As the authors show, the only difference between open and closed drainage is that, in the former, air is allowed to re-enter the empyema cavity, whereas in the latter this is prevented. The fault with the presentation in this book is that some readers will be led to believe that the size and character of the drainage opening determines the type of drainage.

This is a book that everyone interested in thoracic surgery will want to own. Its format and size are such that it can be easily carried, and this reviewer prophesies that many series of residents and young surgeons will make it their constant companion during their work in thoracic surgery. Johnson and Kirby have made a very real contribution to the rapidly growing library on thoracic surgery.

RICHARD H. MEADE.

[1] THE HISTORY AND DEVELOPMENT OF NEUROLOGICAL SURGERY. By Ernest Sachs, A.B., M.D. New York: Paul B. Hoeber, Inc., 1952.

[2] A HANDBOOK OF OPERATIVE SURGERY; SURGERY OF THE CHEST. By Julian Johnson, M.D., D.Sc. (Med.), and Charles E. Kirby, M.D. Chicago: The Year Book Publishers, Inc., 1952.

THE ninth edition of the classical work, *The Treatment of Diabetes Mellitus*,[1] changed little in plan or format, has been thoroughly revised to incorporate present day knowledge of the treatment and nature of diabetes. Stressed are the importance and rewards of continued excellent control of the diabetic patient in preventing vascular degeneration and the value to him of repeated education and re-examination in camps or hospital teaching clinics. While other excellent monographs on diabetes are available none can replace this book which reflects the experience of Joslin and his associates over a period of 54 years. WALTER H. NADLER.

THE book *Lehrbuch der Geburtshilflichen Operationen*[2] which is volume 3 of *Lehrbuch der Geburtshilfe und Gynaekologie* was prepared by 6 coauthors, E. Anderes, E. Glatthaar, M. Laszczower, H. Sauter, H. Willi and H. Winzeler. The subjects discussed are the general aspects of obstetrics, preparations for obstetric operations, operative manipulations during pregnancy, operative procedures during labor, and operative measures during the postpartum period. There is also a special section devoted to complications such as rupture of the uterus, treatment of asphyxia neonatorum, birth injuries of the child, the treatment of hemorrhage, and medicolegal aspects of obstetrics. Because 6 men collaborated, the book is not as smoothly written as if one author wrote the entire book but this is really not a drawback. Each author is well qualified to write his section and in nearly all instances the advice given is in accord with obstetric practice in most countries. However, there are a few points of difference. Laminaria tents for dilatation of the cervix are described and illustrated but these tents are no longer used in the United States. Several methods of sterilization are described and illustrated such as tubal resection and the Madlener technique but the Pomeroy method and the Irving procedure are not mentioned even though these sterilization procedures are among the most reliable ones. The lateral episiotomy shown is a mediolateral one. A large amount of space (23 pages) and too many illustrations (15) are devoted to destructive operations in the child. Six illustrations are used to describe the delivery of a breech by means of a hook, which is a dangerous procedure. The authors describe and illustrate Braxton Hicks version for the treatment of total placenta previa. In my opinion cesarean section is the treatment of choice in all cases of total placenta previa. All the illustrations show bare hands, but in the preface Anderes explains that this was done deliberately for better visualization of technique. However, in all the illustrations the pubic and vulvar hair is shown in its full abundance. There are 175 illustrations, all of them beautiful, clear, and instructive. Many of these are in color.

The authors have written an excellent book, which is full of useful information and sound practical advice. The publishers too have carried out their task admirably. This book will undoubtedly be very popular in German-speaking countries.

J. P. GREENHILL.

THE monograph *Die zerebrale Angiographie*[3] is so well illustrated that even those unable to read German can profit from it. Actually the text is clearly written and amplifies the pictures considerably. After a short historical introduction, there are sections on techniques (largely percutaneous), contrast materials (an equivalent of diodrast has been most often used), and radiography. The normal carotid and vertebral angiograms are then pictured. Common variants and anastomoses are discussed. Succinct chapters on vascular diseases, space-occupying lesions, hydrocephalus, and skull and brain injuries are followed by the atlas proper. This occupies two-thirds of the monograph, and consists of reproductions of roentgenograms, brief case histories, and drawings of the angiograms. These are uniquely done, with different shadings to represent vessels in different planes. This is constant throughout the book, clarifying any obscurities in the roentgenograms. Since the drawings are labeled, the roentgenograms are usually not, to their advantage. The bibliography is extensive and the index is clear.

This volume is a well-made example of the bookmaker's art. The reproductions of angiograms are superb and superior to those in any English language book on angiography thus far published. Anyone engaged in the interpretation of cerebral angiograms should have this book readily available.

OSCAR SUGAR.

THE book *The English Pioneers of Anaesthesia (Beddoes, Davy, and Hickman)*[4] by an eminent English anesthetist presents much interesting and original information on the preliminary work which made possible the clinical introduction of anesthesia. The method of presentation is that of short biographies of the three Englishmen who may be regarded as the progenitors of anesthesia.

The background of the life story of the central figures is effectively pictured in the opening chapters. The period from 1790 to 1830 was a time of change and advancement in science and politics and the practice of pneumatic medicine reached its peak and declined.

[1] THE TREATMENT OF DIABETES MELLITUS. By Elliott P. Joslin, A.M., M.D., Sc.D., Howard F. Root, M.D., Priscilla White, M.D., Sc.D., and Alexander Marble, A.M., M.D. 9th rev. ed. Philadelphia: Lea & Febiger, 1952.

[2] LEHRBUCH DER GEBURTSHILFE UND GYNAEKOLOGIE. By E. Anderes, H. Guggisberg, and Th. Koller. Vol. 3. LEHRBUCH DER GEBURTSHILFLICHEN OPERATIONEN. By Prof. Dr. E. Anderes. Compiled by Prof. Dr. E. Anderes, P.D., Dr. E. Glatthaar, Dr. M. Laszczower, Dr. H. Sauter, Prof. Dr. H. Willi, P.D., and Dr. H. Winzeler. Basel: S. Karger, 1952.

[3] DIE ZEREBRALE ANGIOGRAPHIE. By H. Krayenbühl and Hs. R. Richter. Stuttgart: Georg Thieme, 1952.

[4] THE ENGLISH PIONEERS OF ANAESTHESIA (BEDDOES, DAVY, AND HICKMAN). By F. F. Cartwright. Baltimore: The Williams & Wilkins Co.; Bristol: John Wright & Sons Ltd.; London: Simpkin Marshall Ltd., 1952.

In the biographies are numerous quotations from the writings of the subjects and from contemporary periodicals and literature. The story of the life and work of these pioneers is told largely in their own words and those of their associates. The author's scholarly concluding essay considers the importance of these events in the development of anesthesia. Beddoes attempted to make of pneumatic medicine an exact science and gave Davy his inspiration. Davy stumbled upon the truth and first suggested a practicable means of anesthesia. Hickman's work forms the link which joins the parent pneumatic medicine with the descendant anesthesia.

The material is presented in a compact, attractive publication on good paper with easily readable print. The plates depict portraits of the subjects and their associates and papers from original sources. The bibliography is extensive. All anesthetists will be grateful for this valuable contribution to the history of anesthesia. MARY F. POE.

BOOKS RECEIVED

Books received are acknowledged in this department, and such acknowledgment must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers and as space permits.

TUBERCULOSIS OF BONE AND JOINT. By G. R. Girdlestone and E. W. Somerville, M.B., F.R.C.S. (Ed.). 2nd ed. London, New York: Oxford University Press, 1952.

PHARMACOLOGY IN CLINICAL PRACTICE. By Harry Beckman, M.D. Philadelphia, London: W. B. Saunders Co., 1952.

DIE OSTEOMALAZIE. By Dr. Med. Markus Wernly. Stuttgart: Georg Thieme, 1952.

PICTORIAL HANDBOOK OF FRACTURE TREATMENT. By Edward L. Compere, M.D., F.A.C.S., Sam W. Banks, M.D., F.A.C.S., and Clinton L. Compere, M.D., F.A.C.S. 3rd ed. Chicago: The Year Book Publishers, Inc., 1952.

PHYSICAL FOUNDATIONS OF RADIOLOGY. By Otto Glasser, Edith H. Quimby, Lauriston S. Taylor, and J. L. Weatherwax. 2nd rev. enl. ed. New York: Paul B. Hoeber, Inc., Medical Book Department of Harper & Bros., 1952.

SEX AFTER FORTY. By S. A. Lewin, M.D., and John Gilmore, Ph.D. New York: Medical Research Press, 1952.

CLINICAL PROBLEMS IN CANCER RESEARCH; SLOAN-KETTERING INSTITUTE SEMINAR 1948–1949. By The Sloan-Kettering Institute. New York: The Sloan-Kettering Institute, 1952.

APPLIED PHYSIOLOGY. By Samson Wright, M.D., F.R.C.P. With the collaboration of Montague Maizels, M.D., F.R.C.P., and John B. Jepson, M.A., B.Sc., D.Phil., A.R.I.C. 9th ed. London, New York, Toronto: Oxford University Press, 1952.

CARDIAC THERAPY. By Harold J. Stewart, M.D. New York: Paul B. Hoeber, Inc., Medical Book Department of Harper & Bros., 1952.

STERILITY; ITS CAUSE AND ITS TREATMENT—Part I, THE INFERTILE FEMALE; Part II, THE INFERTILE MALE. By J. Jay Rommer, A.B., Ph.G., M.D., A.I.C.S. Springfield, Ill.: Charles C Thomas, 1952.

RESEARCH IN ENDOCRINOLOGY. By August A. Werner, M.D., and Associates. Edited by Al R. Schmidt, City Editor, Belleville Daily Advocate, Belleville, Illinois.

ANURIE BEI CHROMOPROTEINURIE (HÄMOLYSENIERE, CRUSH-NIERE). By Prof. Dr. Hans U. Zollinger. Stuttgart: Georg Thieme, 1952.

EMERGENCY SURGERY. Part IV. By Hamilton Bailey, F.R.C.S. (Eng.), F.A.C.S., F.I.C.S., F.R.S.E. Assisted by Norman M. Matheson, M.B., Ch.B., M.R.C.P. (Lond.), F.R.C.S. (Eng.), F.A.C.S. 6th ed. Baltimore: The Williams & Wilkins Co., 1952.

INTRACRANIAL ANEURYSMS. By Wallace B. Hamby, M.D. Springfield, Ill.: Charles C Thomas, 1952.

GYNECOLOGIC AND OBSTETRIC PATHOLOGY WITH CLINICAL & ENDOCRINE RELATIONS. By Emil Novak, A.B., M.D., D.Sc. (Hon.), F.A.C.S., F.R.C.O.G. (Hon.). 3rd ed. Philadelphia, London: W. B. Saunders Co., 1952.

PIE VARO EQUINO CONGENITO. By José Alberto Piqué. Buenos Aires: Editorial "Casa Solari," 1952.

OPERATIVE NEUROSURGERY WITH EMPHASIS ON PROCEDURES IN TRAUMA. By Elisha Stephens Gurdjian, M.D., John E. Webster, M.D. Baltimore: The Williams & Wilkins Co., 1952.

THE ESOPHAGUS AND ITS DISEASES. By Eddy D. Palmer, M.D., F.A.C.P. New York: Paul B. Hoeber, Inc., Medical Book Department of Harper & Bros., 1952.

A STEREOSCOPIC ATLAS OF HUMAN ANATOMY. Section I —THE CENTRAL NERVOUS SYSTEM. By David Bassett, M.D., and W. B. Gruber. Portland, Oregon: Sawyer's Inc., 1952.

MAN AGAINST CANCER; THE STORY OF CANCER RESEARCH. By Dr. I. Berenblum. Baltimore: The Johns Hopkins Press, 1952.

HEMATOMAS INTRACRANEANOS TRAUMÁTICOS. By Pedro Larghero. Montevideo: Imp. Rosgal, Hilario Rosillo, 1952.